NORTH ATLANTIC TREATY ORGANIZATION

SCIENCE AND TECHNOLOGY ORGANIZATION

AC/323(HFM-192)TP/664

www.sto.nato.int

STO TECHNICAL REPORT **TR-HFM-192**

Optimal Use of Hyperbaric Oxygen Therapy in Military Medical Setting

(Utilisation optimale de l'oxygénothérapie hyperbare dans le contexte militaire)

The Task Group on Hyperbaric Oxygen Therapy in military medical setting explored the usefulness of hyperbaric oxygenation for medical conditions encountered in operational military settings; taking into account the technical specificities and constraints of hyperbaric oxygen therapy administration, recommendations are made as to the optimal implementation of this treatment.

Published February 2016

NORTH ATLANTIC TREATY ORGANIZATION

SCIENCE AND TECHNOLOGY ORGANIZATION

AC/323(HFM-192)TP/664

www.sto.nato.int

STO TECHNICAL REPORT **TR-HFM-192**

Optimal Use of Hyperbaric Oxygen Therapy in Military Medical Setting

(Utilisation optimale de l'oxygénothérapie hyperbare dans le contexte militaire)

The Task Group on Hyperbaric Oxygen Therapy in military medical setting explored the usefulness of hyperbaric oxygenation for medical conditions encountered in operational military settings; taking into account the technical specificities and constraints of hyperbaric oxygen therapy administration, recommendations are made as to the optimal implementation of this treatment.

The NATO Science and Technology Organization

Science & Technology (S&T) in the NATO context is defined as the selective and rigorous generation and application of state-of-the-art, validated knowledge for defence and security purposes. S&T activities embrace scientific research, technology development, transition, application and field-testing, experimentation and a range of related scientific activities that include systems engineering, operational research and analysis, synthesis, integration and validation of knowledge derived through the scientific method.

In NATO, S&T is addressed using different business models, namely a collaborative business model where NATO provides a forum where NATO Nations and partner Nations elect to use their national resources to define, conduct and promote cooperative research and information exchange, and secondly an in-house delivery business model where S&T activities are conducted in a NATO dedicated executive body, having its own personnel, capabilities and infrastructure.

The mission of the NATO Science & Technology Organization (STO) is to help position the Nations' and NATO's S&T investments as a strategic enabler of the knowledge and technology advantage for the defence and security posture of NATO Nations and partner Nations, by conducting and promoting S&T activities that augment and leverage the capabilities and programmes of the Alliance, of the NATO Nations and the partner Nations, in support of NATO's objectives, and contributing to NATO's ability to enable and influence security and defence related capability development and threat mitigation in NATO Nations and partner Nations, in accordance with NATO policies.

The total spectrum of this collaborative effort is addressed by six Technical Panels who manage a wide range of scientific research activities, a Group specialising in modelling and simulation, plus a Committee dedicated to supporting the information management needs of the organization.

- AVT Applied Vehicle Technology Panel
- HFM Human Factors and Medicine Panel
- IST Information Systems Technology Panel
- NMSG NATO Modelling and Simulation Group
- SAS System Analysis and Studies Panel
- SCI Systems Concepts and Integration Panel
- SET Sensors and Electronics Technology Panel

These Panels and Group are the power-house of the collaborative model and are made up of national representatives as well as recognised world-class scientists, engineers and information specialists. In addition to providing critical technical oversight, they also provide a communication link to military users and other NATO bodies.

The scientific and technological work is carried out by Technical Teams, created under one or more of these eight bodies, for specific research activities which have a defined duration. These research activities can take a variety of forms, including Task Groups, Workshops, Symposia, Specialists' Meetings, Lecture Series and Technical Courses.

The content of this publication has been reproduced directly from material supplied by STO or the authors.

Published February 2016

ISBN 978-92-837-2026-3

Table of Contents

List of Tables

HFM-192 Membership List

LtCol MC Dietmar M. FISCHER, MD
Dept of Anesthesiology and Intensive Care Medicine
Federal Armed Forces Hospital Ulm
Oberer Eselsberg 40
89081 Ulm
GERMANY
Email: mail@decodoc.de / dietmar.fischer@extern.uni-ulm.de / dietmarmanfredfischer@bundeswehr.org

LtCol Peter GERMONPRE, MD (Chair)
Centre for Hyperbaric Oxygen Therapy
Military Hospital Brussels
Rue Bruyn, 1
B-1120 Brussels
BELGIUM
Email: peter.germonpre@mil.be / p.germonpre@gmail.com

CFR MN Franscisco GUERREIRO, MD
Hospital das Forças Armadas
Azinhaga Ulmeiros
1620-060 Lisboa
PORTUGAL
Email: quaresma.guerreiro@marinha.pt / franciscogamitoguerreiro@gmail.com / fransciscoguerreiro@iol.pt

ADC Robert HOUMAN, CHT
(Retired from RTG-192 as of January 2012)
Centre for Hyperbaric Oxygen Therapy
Military Hospital Brussels
Rue Bruyn, 1
B-1120 Brussels
BELGIUM
Email: rob.houman@mil.be

Dr. Igor MEKJAVIC
(Until 2012 – not replaced)
Institute Jozef Stefan
Jamova 39
1000 Ljubljana
SLOVENIA
Email: igor.mekjavic@ijs.si

Capt Mark E. MICHAUD
(As from 2012)
Bureau of Medicine and Surgery
Head, Undersea Medicine and Radiation Health (M3B3)
2300 E Street, NW
Washington, DC
UNITED STATES
Email: Mark.Michaud@med.navy.mil

Mesut MUTLUOGLU, MD
(As from 2013)
Department of Underwater and Hyperbaric Medicine
Gulhane Military Medical Academy
Haydarpasa Teaching Hospital
34668, Uskudar, Istanbul
TURKEY
Email: drmutluoglu@gmail.com

Milos SAZEL, MD, PhD, LtCol. ret.
Institute of Aviation Medicine Prague
Gen. Piky 1
P.O. Box 19
160 60 Prague 6
CZECH REPUBLIC
Email: sazel@ulz.cz / sazel@centrum.cz

LT(N) Gunalp UZUN, MD
Assistant Professor
Department of Underwater and Hyperbaric Medicine
Gulhane Military Medical Academy
Haydarpasa Teaching Hospital
34668, Uskudar, Istanbul
TURKEY
Email: gunalpuzun@gmail.com

Edward (Andy) WOODS Captain MC, USN
BUMED M3/5 Director Fleet Programs
Specialty Leader Undersea Medicine and Radiation Health
2300 E Street NW
Washington, DC 20372-5300
UNITED STATES
Email: edward.woods@med.navy.mil

Optimal Use of Hyperbaric Oxygen Therapy in Military Medical Setting

(STO-TR-HFM-192)

Executive Summary

Hyperbaric oxygen therapy is the treatment of patients with oxygen breathing while in a pressurized treatment chamber. The increased oxygen transport and delivery to the tissues has beneficial effects in a variety of diseases and conditions, some of which are pertinent to military (battlefield) injury. When administered timely and in a correct way, hyperbaric oxygen therapy improves the evolution and final outcome; however, because of the technical limitations of the treatment (necessity of a hyperbaric treatment chamber, of adequate oxygen and compressed air supplies, of competent medical and paramedical personnel), hyperbaric oxygen therapy centres are not very common, even in non-military setting.

This Task Group examined the possible military applications of hyperbaric oxygen therapy, and defined the conditions for its use. It appeared that while it is not realistic to suggest the placement of hyperbaric treatment centres close to operations theatres, it may be possible to organise the medical evacuation routes in such a way that military patients can be treated before returning to their homeland in a (civilian or military) hyperbaric centre "along the route", for a short period, before being further evacuated to their final destination. This way, a rapid evacuation from the operations theatre could be combined with a timely hyperbaric treatment, thereby shortening total treatment time and optimising final recovery.

The surrounding conditions for hospitals with hyperbaric oxygen therapy centres have been defined. For a hyperbaric treatment to be effective, it is necessary that adjunctive therapies and medical conditions are optimal for the pathology. Centres can thus be classified as belonging to various categories of hospitals, and for each pathology, an appropriate hospital category has been defined. This must allow medical planners to design evacuation routes according to the expected case load.

Finally, the Task Group proposes further actions to be taken in order to aid medical planners in designing the appropriate evacuation routes, and has identified appropriate hospitals and knowledgeable contact persons in most NATO Nations.

Utilisation optimale de l'oxygénothérapie hyperbare dans le contexte militaire

(STO-TR-HFM-192)

Synthèse

L'oxygénothérapie hyperbare consiste à traiter les patients en leur faisant respirer de l'oxygène dans un caisson pressurisé. Le transport et l'apport accrus d'oxygène aux tissus a des effets bénéfiques sur diverses maladies et divers états, pertinents pour certaines blessures reçues sur le champ de bataille. Lorsqu'elle est appliquée correctement et en temps opportun, l'oxygénothérapie hyperbare améliore l'évolution de la maladie et le résultat final. Cependant, étant donné les contraintes techniques de ce traitement (nécessité d'un caisson hyperbare, d'un approvisionnement adéquat en oxygène et en air comprimé et de personnel médical et paramédical compétent), les centres d'oxygénothérapie hyperbare ne sont pas très courants, même hors du contexte militaire.

Ce groupe de travail a examiné les applications militaires possibles de l'oxygénothérapie hyperbare et en a défini les conditions d'utilisation. Il est apparu que, même s'il n'est pas réaliste de suggérer l'implantation de centres de traitement hyperbare près des théâtres des opérations, il serait possible d'organiser les trajets d'évacuation sanitaire de façon à ce que les patients militaires puissent être traités avant de rentrer dans leur pays, dans un centre hyperbare civil ou militaire « sur le chemin », pendant une courte période, avant d'être évacués jusqu'à leur destination finale. Ainsi, une évacuation rapide du théâtre des opérations pourrait être associée à un traitement hyperbare en temps opportun, ce qui raccourcirait la durée totale du traitement et optimiserait la récupération.

Les conditions associées des hôpitaux équipés de centres d'oxygénothérapie hyperbare ont été définies. Un traitement hyperbare efficace passe par des thérapies auxiliaires et des conditions médicales optimales pour la pathologie en question. Les centres entrent par conséquent dans diverses catégories d'hôpitaux et pour chaque pathologie, une catégorie appropriée a été définie. Cela doit permettre aux planificateurs médicaux de concevoir des trajets d'évacuation en fonction du nombre de cas attendus.

Pour finir, le groupe de travail propose des mesures supplémentaires afin d'aider les planificateurs médicaux à concevoir des trajets d'évacuation appropriés et identifie des hôpitaux adéquats et les interlocuteurs compétents dans la plupart des nations de l'OTAN.

Chapter 1 – BACKGROUND AND JUSTIFICATION

1.1 HYPERBARIC OXYGEN THERAPY

Hyperbaric Oxygen Therapy (HBO) has been used for the treatment of various diseases and illnesses since the 1960's. Its use has been progressively expanding, based on experience and scientific studies. It is recognized that these scientific studies are difficult to perform and are generally not unequivocally accepted as "solid scientific proof" – this is partly due to the scarceness and variability of the diseases studied, but also to the lack of suitable therapeutic alternatives for many of these, hindering proper randomization and "sham control". Also, the use of specific technical apparatus (the hyperbaric chamber) renders "blinding" of patients difficult if not impossible. Finally, the lack of commercial or government (social security) funding has kept the number of hyperbaric treatment facilities low, and the quality of care delivered in these, variable.

HBO involves respiration of pure oxygen under high atmospheric pressure. In order to be able to breathe any gas at pressures higher than 1 atmosphere, patients must be exposed to the same pressure externally – hence the need for a hyperbaric treatment "chamber" – essentially a pressure vessel.

While smaller and older hyperbaric chambers were filled with pressurized oxygen, most hyperbaric chambers today are using compressed air, while patients breathe oxygen via an orofacial mask, a "hood" (a clear plastic head tent) or via a tracheostomy tube or endotracheal tube.

Guidelines for HBO have been developed by "Scientific Societies", both in the USA (Undersea and Hyperbaric Medical Society – UHMS) and Europe (European Committee for Hyperbaric Medicine – ECHM). These guidelines encompass both the selection of patients ("Indications for Hyperbaric Oxygen Therapy") and the proper execution of the treatment ("Code of Good Clinical Practice").

1.2 ACCEPTED INDICATIONS FOR HBO

The close link with diving, aviation and space medicine has made hyperbaric medicine slightly better known with the general public over the last couple of years. Most of the clinical applications however lie in the field of complex trauma (combined vascular, muscular and neurological injury), anaerobic infections (gas gangrene), enhancement of wound-healing, decompression illness, acute acoustic trauma and carbon monoxide intoxication. All of these diseases or conditions require (often) urgent, comprehensive (multi-disciplinary) hyperbaric treatment to ensure a maximal efficiency.

Although for very few HBO indications a sufficient body of "level I" scientific evidence seems to be present to unequivocally have the treatment modality "accepted" by the entire medical community, "lower levels" of scientific evidence combined with physiological logic and "common sense" have resulted in periodically reviewed guidelines issued by the hyperbaric Scientific Societies. These can be downloaded from their respective websites (www.uhms.org; www.echm.org). A summary is listed below.

Table 1-1: Accepted Indications for HBO According to ECHM (Source: [www.achobel.be]).

CONDITION	ACCEPTED			NOT ACCEPTED		
	Level of Evidence			Level of Evidence		
	A	B	C	D	E	F
Type I						
CO intoxication		X				
Crush Syndrome		X				
Prevention of Osteoradionecrosis (dental extraction)		X				
Osteoradionecrosis (mandible)		X				
Soft Tissue Radionecrosis (cystitis)		X				
Decompression Accident			X			
Gas Embolism			X			
Anaerobic or Mixed Bacterial Anaerobic Infections			X			
Type II						
Diabetic Foot Lesion		X				
Compromised Skin Graft and Musculocutaneous Flap			X			
Osteoradionecrosis (other bones)			X			
Radio-induced Proctitis / Enteritis			X			
Radio-induced Lesions of Soft Tissues			X			
Surgery and Implant in Irradiated Tissue (preventive action)			X			
Sudden Deafness			X			
Ischemic Ulcer			X			
Refractory Chronic Osteomyelitis			X			
Neuroblastoma Stage IV			X			
Type III						
Post-anoxic Encephalopathy			X			
Larynx Radionecrosis			X			
Radio-induced CNS Lesions			X			
Post-vascular Procedure Reperfusion Syndrome			X			
Limb Re-implantation			X			
Burns >20 % of Surface Area and 2nd degree			X			
Acute Ischemic Ophthalmologic Disorders			X			
Selected Non-healing Wounds secondary to Inflammatory Processes			X			
Pneumatosis Cystoides Intestinalis			X			
Other indications						
Post-sternotomy Mediastinitis				X		
Stroke				X		
Sickle Cell Disease				X		
Malignant Otitis Externa				X		
Acute Myocardial Infarction				X		
Femoral Head Necrosis				X		
Retinitis Pigmentosa					X	
Tinnitus					X	
Interstitial Cystitis					X	
Facial (Bell's) Palsy					X	
Cerebral Palsy						X
Multiple Sclerosis						X
Fetoplacental Insufficiency						X

- Level A: At least 2 concordant, large, double-blind, controlled randomized studies with no or little methodological bias.
- Level B: Double-blind controlled, randomized studies but with methodological flaws; studies with only small samples, or only a single study.
- Level C: Consensus opinion of experts.
- Level D: Only uncontrolled studies with no consensus opinion of expert.
- Level E: No evidence of beneficial action, or methodological or interpretation bias preclude any conclusion.
- Level F: Existing evidence favors not to use HBO_2.

Table 1-2: "Accepted Indications" for HBO According to UHMS (Source: [www.uhms.org]).

1) Air or Gas Embolism
2) Carbon Monoxide Poisoning
3) Carbon Monoxide Poisoning Complicated by Cyanide Poisoning
4) Clostridial Myositis and Myonecrosis (Gas Gangrene)
5) Crush Injury, Compartment Syndrome and Other Acute Traumatic Ischemias
6) Decompression Sickness
7) Arterial Insufficiencies:
    - Central Retinal Artery Occlusion
    - Enhancement of Healing in Selected Problem Wounds
8) Severe Anaemia
9) Intracranial Abscess
10) Necrotizing Soft Tissue Infections
11) Osteomyelitis (Refractory)
12) Delayed Radiation Injury (Soft Tissue and Bony Necrosis)
13) Compromised Grafts and Flaps
14) Acute Thermal Burn Injury
15) Idiopathic Sudden Sensorineural Hearing Loss

1.3 SPECIFIC MILITARY INDICATIONS

Whereas many "chronic" indications have no military specificity, the nature of warfare provides for some injuries which can be classified as "ideal candidates" for hyperbaric treatment. Indeed, trauma with combined bone/soft tissue/neurological injuries and often vascular compromise, infected wounds, decompression illness, altitude illness, thermal burns, carbon monoxide intoxication are frequent consequences of military activity in operation.

1.4 COMPLEXITY OF HBO IN MILITARY SETTINGS

Both European and US scientific hyperbaric organizations have confirmed that complex trauma care needs to be performed in a multi-disciplinary setting. Because of the often complex concomitant therapy needed, it would be necessary to direct these patients immediately to the most appropriate hospital offering both HBO and, for example, neurosurgery, trauma care or burn care. The optimal use of HBO and specialized care will result in a faster recovery and a reduction of overall treatment costs.

The relative isolation of military operation theatres, both geographically and because of enemy activity, makes this optimal "treatment path" difficult and often impossible. Hyperbaric chambers can (often) not be deployed close to the injury site (exception made perhaps for ship-mounted HBO chambers for diving operations support), so a primary evacuation to an optimal "combined facility" is, in the vast majority of cases, not possible. However, a "therapeutic window" can be defined, within which HBO should be started, and attempts should be made to ensure this therapeutic time-frame can be met. Multi-national cooperation, as exists already for military operations, including medical support on-site and for evacuation, is the key to this.

Chapter 2 – OBJECTIVES OF THIS REPORT

2.1 DEFINE MILITARY INDICATIONS FOR HBO

Whereas military personnel can benefit from HBO as part of classical healthcare when residing in their home country, the use of this treatment in case of injuries and diseases suffered while on deployment is seriously hampered by logistical difficulties and medical prioritizing. However, it appears that many combat-related injuries could, at least theoretically, benefit substantially from hyperbaric treatment if installed within the useful early timeframe. It has been the objective of this Working Group to define the medical conditions potentially encountered in operations, and also the optimal time frame during which addition of HBO to the "normal" care may be beneficial. The summaries and rationale can be found below and in Annex A.

2.2 DEFINE "CONDITIONS FOR USE"

Furthermore, as the addition of any treatment modality cannot be allowed to compromise the quality of the "usual care", a list of conditions has been formulated for each indication, helping Medical Planning staff to decide whether this is a "viable" option.

In the modern military setting, many if not most of these diseases would happen in remote operational theatres and rapid and coordinated evacuation of these patients to the optimal higher echelon treatment centre is essential. It is unlikely that fully functional military HBO centres can be deployed in close proximity of the operational theatre (bar exceptions, see below), meaning that HBO should be administered early in the evacuation chain back to the home country.

Although in most NATO Nations, at least one military hyperbaric centre is available, either in-hospital or in a stand-alone (e.g. naval) setting, few of those centres can offer the various aspects of multi-disciplinary care. This implies that wounded soldiers will often not be evacuated to the best treatment facility, and only receive partial care. Although the need for hyperbaric readiness and coordination plans is partially addressed in the context of Submarine Escape and Rescue (SMER) planning, a more general approach is needed to encompass other indications for HBO.

Also, there is as yet no formal coordination between the various NATO Nations' military hyperbaric centres, neither regarding clinical protocols nor operating or safety procedures, nor personnel training and education. Because of this lack of interoperability, collaboration in the context of multi-national operations is difficult to organize.

By working towards a concerted action, NATO Nations will be able to specifically focus the available hyperbaric medicine capacity of each member nation towards an optimal utilization in times of need. More practical, patients referred to one of the Member Nation's hyperbaric centres will be guaranteed a standardized approach, both medical and administrative, and will thus minimize the time to optimal treatment, and reduce medical and evacuation costs for each NATO Nation.

Among the "conditions for use", criteria have been developed to aid in identifying the suitable hospitals with (military and civilian) HBO facilities beforehand, so that evacuation routes, military-medical supervision and financial agreements may be elaborated during the planning phase of the medical support operation.

2.3 PROPOSE PROCEDURE FOR TREATMENT OF MILITARY INJURIES

Finally, this report will propose a "general workflow" for HBO treatment of military injuries, which can serve as a framework onto which specific procedures can be developed. Also, it is proposed to organize a

"Lecture Series" for military (para)medical NATO personnel, with the aim of providing a basic knowledge of HBO and its potential use in military setting.

Chapter 3 – MILITARY INDICATIONS*

For each of the following diseases or conditions, the relevant characteristics have been summarized. Diseases and conditions have been listed roughly alphabetically; the order of discussion does not reflect relative importance or frequency of occurrence.

Annex A elaborates for each condition the scientific rationale and available evidence. Because this report does not pretend to be scientifically complete, reference is made to published reviews.

DEFINITIONS USED IN THIS SUMMARY

Vital or Non-Vital Emergency

Determines whether the condition, or its immediate to short-term evolution, may or may not compromise the victim's life. Conditions that may have a severe functional impact (e.g. necessitating major amputations) are – in this military operational setting – NOT CLASSIFIED as "life-threatening" – this is opposed to standard NATO P-classification (see below).

Maximum Delay of Useful HBO Therapy for this Condition

Determines directly the decision to evacuate or not, depending on the local possibilities. If HBO is started beyond this time point, the added benefit of the treatment probably does not outweigh the extra effort or (healthcare or tactical) risks of evacuating the patient.

Condition of Evacuation

Here, NATO classification is adhered to, as far as Priority (NATO Priority – P-factor) and Medical Support needed (NATO Dependency – D-factor). Also, special considerations for transport may be listed.

NATO Priority

P1 Life-threatening: life, limb, eyesight

Aircraft launch < 12 hrs – pt return to Europe < 24 hrs

P2 Priority

Aircraft launch < 24 hrs – pt return 24 – 48 hrs

P3 Routine

Aircraft launch > 24 hrs

NATO Dependency

D1 – Full intensive care support (ICU) needed

D2 – Intermediate care (full monitoring, perfusions, drains, etc.) needs (para)medical care during flight

D3 – Low care (urine catheter, IV, pain meds, etc.) need (para)medical attention

D4 – No care (ambulatory)

* See also Annex A.

Conditions for HBO Therapy

In this item is determined whether the HBO treatment should be performed (or capable of being performed) with intensive care support (ICU) or not; whether the patient would be mandatorily hospitalized for care or could be ambulatory; and finally an estimate of the expected maximal duration of emergency HBO – after this, the patient either would not need further HBO or could be transferred further, implying an interruption of daily HBO for a number of days.

Minimal Specialized Medicine Needed

As HBO is in many cases an adjunctive treatment, it is important that patients receive proper "classical" medical care as a priority. Whether this "specialized medical care" is needed on site – in the institution/ hospital that provides HBO – or not (available for outpatient consultation), is listed in the next item.

Type of Hyperbaric Facility (see CGP)

Reference is made here to the definitions of HBO facilities as described in the European Code of Good Practice (CGT) in HBO, published by ECHM and available for download on www.echm.org. In short, a hyperbaric chamber system consists of the hyperbaric chamber(s) including the support equipment (gas and energy supplies, etc.). A hyperbaric facility consists of the therapeutic hyperbaric system(s) together with associated plant, buildings, staff (both technical and medical), and a specific administrative organization. Two kinds of hyperbaric facilities exist:

- Hospital based; and
- Standalone.

However, in each and every hyperbaric facility there should be an area adequately equipped to receive and care for medical emergencies. A Centre for Hyperbaric Medicine is a medical facility that provides HBO for patients and additional treatments, surveillance and attention to the medical conditions of the patient. The centre for hyperbaric medicine must be physically located in or functionally linked to a hospital.

Recommended HBO Protocol

Although pressure and duration of HBO sessions may vary dependent on the country, local possibilities and personal rationale, it is possible to define a "standard" HBO session as:

- Having a duration of minimum 60 minutes of oxygen breathing at pressure (Note: Commonly used protocols have between 70 – 90 minutes of oxygen breathing).
- At a pressure of minimum 2.4 atmospheres absolute pressure (ATA) (Note: Commonly used protocols vary between 2.4 and 2.5 ATA).
- With a maximum of two "air breaks" during the session (short periods where the oxygen mask or hood is taken off, so that the patient can breathe freely, but breathes air, not oxygen).

For diving emergencies and certain anaerobic infections, different schedules are available, and this is indicated when appropriate. The frequency and duration of HBO, as well as short recommendations for adjunctive treatments that are considered essential are given.

Directions for Future Research

As indicated above, often there is only a limited volume of high-grade scientific evidence for the efficacy of HBO in these (any) conditions. The treatment of military patients presents a unique opportunity to increase the data volume, and contribution of patient data to existing registries should be done whenever possible.

In case no specific data collection exists, it is recommended to document each case as completely as possible, for future pooling and analysis.

3.1 ACOUSTIC TRAUMA

i) *Vital or non-vital emergency?*

Non-vital.

ii) *Maximum delay of useful HBO therapy for this condition?*

HBO treatment should be started < 48 hrs.

iii) *Condition of evacuation?*

a) P3 (but P2 if already available transport < 48 hrs); and

b) D4.

iv) *Conditions for HBO therapy:*

a) Type of HBO sessions (ICU or non ICU): Non ICU;

b) Status of patient: Ambulatory; and

c) Expected duration of emergency HBO: < 10 days.

v) *Minimal specialized medicine needed:*

ENT.

vi) *Specialized medicine needed on site:*

None.

vii) *Type of hyperbaric facility (see CGP):*

Facility.

viii) *Recommended HBO protocol:*

a) 1 standard HBO treatment per day; and

b) Add treatment with high dose cortisone from day 1.

ix) *Scientific rationale – see Annex A.*

x) *Directions for future research:*

Inclusion in on-going RCT on AAT (Pilot: Centre for Hyperbaric Oxygen Therapy, Brussels, Belgium – medhyper@mil.be).

3.2 (IATROGENIC) ARTERIAL GAS EMBOLISM

i) Vital or non-vital emergency?

Vital.

ii) Maximum delay of useful HBO therapy for this condition?

HBO treatment should be started ASAP, < 48 hrs.

iii) Condition of evacuation?

a) Priority = Life-saving interventions; and

b) P2 – D1 Emergency evacuation.

iv) Conditions for HBO therapy:

a) Type of HBO sessions (ICU or non ICU): ICU;

b) Status of patient: ICU hospitalization; and

c) Expected duration of emergency HBO: 2 – 3 days.

v) Minimal specialized medicine needed:

Intensive care.

vi) Specialized medicine needed on site:

Intensive care.

vii) Type of hyperbaric facility (see CGP):

Centre.

viii) Recommended HBO protocol:

USN TT6 or equivalent.

ix) Scientific rationale – see Annex A.

x) Directions for future research:

Collect clinical data in systematic way.

3.3 BURN INJURY – LIFE-THREATENING (HIGH TBSA OR RESPIRATORY BURNS)

i) Vital or non-vital emergency?

Vital.

ii) Maximum delay of useful HBO therapy for this condition?

HBO treatment should be started within 12 hrs, or not at all (Forward or Tactical Evacuation only).

iii) Condition of evacuation?

a) P1/P2 – D1; and

b) Emergency evacuation: prioritization = life-saving, not HBO.

iv) Conditions for HBO therapy:

a) Type of HBO sessions (ICU or non ICU): ICU;

b) Status of patient: ICU Burn ward hospitalization; and

c) Expected duration of emergency HBO: 3 – 4 days.

v) Minimal specialized medicine needed:

Burn centre.

vi) Specialized medicine needed on site:

Burn centre.

vii) Type of hyperbaric facility (see CGP):

Centre.

viii) Recommended HBO protocol:

2 standard HBO sessions per day for the first 2 – 3 days.

ix) Scientific rationale – see Annex A.

x) Directions for future research:

a) Collect clinical data in systematic way; and

b) Data collection coordination between participating burn centers (outcome parameters comparison between HBO and non-HBO treated patients).

3.4 BURN INJURY – NON-LIFE-THREATENING

i) Vital or non-vital emergency?

Non-vital.

ii) Maximum delay of useful HBO therapy for this condition?

HBO treatment should be started ASAP, < 5 days.

iii) Condition of evacuation?

a) P2 – D2 – D3; and

b) Emergency evacuation only if risk of permanent disability (face, hands, perineum).

iv) Conditions for HBO therapy:

a) Type of HBO sessions (ICU or non ICU): Non ICU;

b) Status of patient: Burn ward hospitalization; and

c) Expected duration of emergency HBO: < 7 days.

v) Minimal specialized medicine needed:

Burn specialist.

vi) Specialized medicine needed on site:

None.

vii) Type of hyperbaric facility (see CGP):

Facility.

viii) Recommended HBO protocol:

2 standard HBO sessions / day if possible.

ix) Scientific rationale – see Annex A.

x) Directions for future research:

a) Collect clinical data in systematic way; and

b) Data collection coordination between participating burn centers (outcome parameters comparison between HBO and non-HBO treated patients).

3.5 CARBON MONOXIDE POISONING (WHERE HBO IS INDICATED – SEE SCIENTIFIC RATIONALE)

i) Vital or non-vital emergency?

Vital, in case of evidence of end-organ dysfunction

a) Impaired consciousness;

b) Cardiac instability with/without ECG ischemic changes;

c) Metabolic acidosis; and

d) Pregnancy (with evidence of foetal distress, or prolonged > 1 hour symptomatic maternal intoxication).

ii) Maximum delay of useful HBO therapy for this condition?

6 hrs from diagnosis and initiation of treatment with normobaric oxygen.

iii) Condition of evacuation?

Emergency evacuation (Forward and Tactical Evacuation only); and

Provide 100% oxygen as soon as possible and during transfer.

iv) Conditions for HBO therapy:

a) Type of HBO sessions (ICU or non ICU): ICU;

b) Status of patient: Hospitalized (medium care or ICU); and

c) Expected duration of emergency HBO: < 2 days.

v) Minimal specialized medicine needed:

Emergency medicine.

vi) Specialized medicine needed on site:

Emergency medicine.

vii) Type of hyperbaric facility (see CGP):

Facility.

viii) Recommended HBO protocol:

a) Standard HBO protocol, 1 or 2 sessions depending on the neurologic recovery. In case a treatment pressure of 3 ATA is possible to achieve, this might be preferred;

b) Consider combined toxicological exposure (cyanide, alcohol, etc.) and treat accordingly; and

c) Recommend formal neurologic follow-up for late neurological effects.

ix) Scientific rationale – see Annex A.

x) Directions for future research:

Collect clinical data in systematic way.

3.6 CRUSH INJURY (COMBINED TRAUMA TO BONES, SOFT TISSUE, VESSELS, OR NERVES)

i) Vital or non-vital emergency?

Non-vital.

ii) Maximum delay of useful HBO therapy for this condition?

HBO treatment should be started at maximum 48 hrs.

iii) Condition of evacuation?

Emergency evacuation only if risk of permanent disability P2 – D2 D3.

iv) Conditions for HBO therapy:

a) Type of HBO sessions (ICU or non ICU): Non ICU (but depends on general condition);

b) Status of patient: Hospitalized (surgery ward); and

c) Expected duration of emergency HBO: < 7 days.

v) Minimal specialized medicine needed:

Trauma centre.

vi) Specialized medicine needed on site:

No, unless life-threatening injury.

vii) Type of hyperbaric facility (see CGP):

Depends on the condition of the patient.

viii) Recommended HBO protocol:

2 standard HBO treatments / day for 2 – 3 days, then 1 treatment / day.

ix) Scientific rationale – see Annex A.

x) Directions for future research:

a) Collect clinical data in systematic way;

b) Classify patients according to international trauma scores (Gustilo); and

c) Adding (anonymous) data to German Trauma Net database (Coordinator: Centre for Hyperbaric Oxygen – Military Hospital Ulm, Germany).

3.7 DECOMPRESSION SICKNESS – LIFE-THREATENING

i) Vital or non-vital emergency?

Vital.

ii) Maximum delay of useful HBO therapy for this condition?

HBO treatment should be started ASAP, < 48 hrs.

iii) Condition of evacuation?

a) P1 – D1 Emergency evacuation indicated (Forward and Tactical Evacuation); and

b) Transfer with 100% oxygen and maximum pressurization (< 1000 ft cabin altitude).

iv) Conditions for HBO therapy:

a) Type of HBO sessions (ICU or non ICU): ICU;

b) Status of patient: Hospitalized ICU; and

c) Expected duration of emergency HBO: < 7 days.

v) Minimal specialized medicine needed:

Intensive care.

vi) Specialized medicine needed on site:

Intensive care.

vii) Type of hyperbaric facility (see CGP):

Centre.

viii) Recommended HBO protocol:

a) Follow directions in ADivP 2;

b) Minimum treatment pressure 2.8 ATA; and

c) Aggressive fluid management needed.

ix) Scientific rationale – see Annex A.

x) Directions for future research:

Collect clinical data in systematic way.

3.8 DECOMPRESSION SICKNESS – NON-LIFE-THREATENING

i) Vital or non-vital emergency?

Non-vital.

ii) Maximum delay of useful HBO therapy for this condition?

HBO treatment should be started ASAP, < 5 days.

iii) Condition of evacuation?

a) P2 – 3 – D2 – 3 (Emergency evacuation only if risk of permanent disability); and

b) Transfer while breathing 100% oxygen and cabin altitude restriction (< 1500 ft cabin pressure).

iv) Conditions for HBO therapy:

a) Type of HBO sessions (ICU or non ICU): Non ICU;

b) Status of patient: Preferably in-patient; and

c) Expected duration of emergency HBO: < 3 days.

v) Minimal specialized medicine needed:

Medical imaging (chest X-ray) (MS: why? pulm. barotrauma then 2).

vi) Specialized medicine needed on site:

None.

vii) Type of hyperbaric facility (see CGP):

Facility.

viii) Recommended HBO protocol:

a) Follow directions in ADivP 2; and

b) Minimum treatment pressure 2.8 ATA.

ix) Scientific rationale – see Annex A.

x) Directions for future research:

a) Collect clinical data in systematic way; and

b) Implement or at least, collect sufficient clinical data, to categorize patients according to different injury severity scoring systems (e.g. the Boussuges scale scoring system for DCS).

3.9 FROSTBITE

i) *Vital or non-vital emergency?*

Non-vital.

ii) *Maximum delay of useful HBO therapy for this condition?*

HBO treatment should be started within 2 – 3 days.

iii) *Condition of evacuation?*

P2 – D2 D3.

iv) *Conditions for HBO therapy:*

a) Type of HBO sessions (ICU or non ICU): non ICU;

b) Status of patient: In-patient; and

c) Expected duration of emergency HBO: 5 – 7 days.

v) *Minimal specialized medicine needed:*

Surgery.

vi) *Specialized medicine needed on site:*

No.

vii) *Type of hyperbaric facility (see CGP):*

Facility.

viii) *Recommended HBO protocol:*

2 standard HBO treatments /day for 2 – 3 days, then once daily.

ix) *Scientific rationale – see Annex A.*

x) *Directions for future research:*

Collect clinical data in systematic way.

3.10 SOFT TISSUE INFECTIONS – LIFE-THREATENING

i) Vital or non-vital emergency?

Vital.

ii) Maximum delay of useful HBO therapy for this condition?

HBO treatment should be started ASAP, < 48 hrs.

iii) Condition of evacuation?

P1 – D1.

iv) Conditions for HBO therapy:

a) Type of HBO sessions (ICU or non ICU): ICU;

b) Status of patient: Hospitalized in ICU department; and

c) Expected duration of emergency HBO: 7 days.

v) Minimal specialized medicine needed:

a) Intensive care with infectious isolation; and

b) (Septic) surgery.

vi) Specialized medicine needed on site:

a) Intensive care; and

b) (Septic) surgery.

vii) Type of hyperbaric facility (see CGP):

Centre.

viii) Recommended HBO protocol:

a) Boerema schedule (3 ATA) if gas gangrene suspected and patient in vital compromise for the first session;

b) 2 standard HBO treatments / day for 2 – 3 days, then 1 treatment / day; and

c) Bacterial culture in order to adapt antibiotic treatment accordingly (anaerobic germs!).

ix) Scientific rationale – see Annex A.

x) Directions for future research:

a) Collect clinical data in systematic way; and

b) Gram test on wound fluid should be reported.

Chapter 4 – CONDITIONS FOR OPTIMAL USE*

In order to aid Medevac Planners in selecting appropriate HBO treatment facilities based on the summary listing above, a description has been provided of the necessary capabilities of a HBO Centre. This will enable a selection of HBO facilities by type of indication, permitting a quick evaluation whether evacuation for HBO is feasible and practical.

First, the definition of "hospital-based" HBO chambers need further detail. The categories of HBO chambers, as defined in the CGP, fall slightly short on the actual characteristics: a Hyperbaric Facility may or may not be "hospital-based", and the next category would then be a "Centre for Hyperbaric Medicine".

For the purpose of military HBO indications, four categories have been defined:

0) The HBO Facility is located outside of the premises of a hospital, or physically distant on the hospital grounds (e.g. another building on the hospital campus grounds) so that ambulance transport is necessary to bring the patient from the ward to the HBO Facility.

I) The HBO Facility is based in a small, local hospital, which may or may not have a limited intensive care facility, but without the possibility of intensive care support during the HBO.

II) The HBO Facility/Centre is based in a larger, regional hospital with full EMS (emergency medical services) and intensive care ward(s); intensive care support is possible during HBO.

III) The HBO Facility/Centre is based in a larger hospital as in II), but the hospital provides additional specialized care.

Intensive care support during HBO needs to be defined as well; for the purpose of this document, a working definition of "ICU HBO" has been made:

- A mechanical ventilator for providing artificial respiration is placed inside the HBO chamber, and is adapted or designed for functioning in hyperbaric environments;
- Hyperbaric-tested or -designed drug infusion pump(s) are placed inside the HBO chamber;
- During the HBO, a minimum of the following patient parameters can be monitored continuously: ECG, blood pressure;
- Arterial Blood Gas measurements can be taken inside the HBO chamber, during treatment, and can be analyzed on-site;
- ICU-competent HBO personnel (as defined in the EBAss curriculum for HBO-ICU-nurse – www.ebass.org – or an ICU-competent MD) is present inside the HBO chamber during the complete treatment; and
- Advanced Life Support (ALS) equipment is readily available at the site of the HBO chamber.

Finally, for each condition discussed above, the required hospital capabilities can be defined.

* See also Annex B.

Table 4-1: Required Hospital Capabilities for Treatment of Military HBO Indications.

Condition	Hosp Based (0 – I – II – III)	ICU HBO	24/24 HBO	7/7 HBO	Special "Capabilities" of the Treating Hospital
1) Acoustic Trauma	0	–	–	+	–
2) Iatrogenic AGE	II	+	+	+	
3) Burns – Life-threatening	III	+	+	+	Burn Centre
4) Burns – Non-life-threatening	0	-	+	+	III – Burn Centre
5) CO-intoxication	I or II	– or +	+	+	
6) Crush	0 or III	– or +	+	+	III – Trauma Centre
7) DCS – Life-threatening	II	+	+	+	
8) DCS – Non-life-threatening	0	–	+	+	–
9) Frostbite (extremities)	0	–	–	+	Surgery
10) Soft Tissue Infections – Life-threatening	III	+	+	+	Septic Surgery

Annex B lists the hospitals that have been identified as of December 2012 with their capabilities to treat the indications/conditions discussed above. This list is not necessarily complete and not static, meaning that it can only serve as a starting point for Evacuation Planners to identify for each projected military support contingency plan the most appropriate HBO Facility and hospital.

Annex C lists contact information for regional or national reference persons/institutions in order to provide a quick and easy way for obtaining up-to-date information regarding existence and availability of these HBO Centres. Likewise, Annex C needs to be updated itself as time goes by, however, web links may persist for a longer time.

Chapter 5 – RECOMMENDATIONS

5.1 PLANNING

On NATO level, Nations usually either perform planning and Airevac operations with their own means and assets, or collaborate in a more or less structured way with partner Nations for "burden sharing". This can be only for a specific mission or on a more permanent basis. An example is the AECC (Aeromedical Evacuation Control Centre) set up within EATC (European Air Transport Command), a multi-national command (Netherlands, Belgium, France, Germany and Luxemburg) established in 2010 with the goal of providing a single headquarters for air transport, air-to-air refueling and aeromedical evacuation, thus setting an example of successful military pooling and sharing in Europe. Within EATC, the AECC is capable of planning and executing medical evacuations is a fast and efficient way. Within the participating Nations, a PECC (Patient Evacuation Control Centre) is both at the "requesting end" and at the "receiving end" of the patient evacuation chain, with AECC organizing the most efficient means and schedule of transport.

Whether the contingency plan for medical evacuation is established through EATC/AECC or independently by individual NATO Nations, preliminary contacts should be made between the (military or civilian) HBO centers and the military Medevac Planner.

As "emergency transfer for HBO" needs to be considered a "primary" emergency, this should possibly be included in existing NATO agreements between partners.

As the medical-surgical and HBO capabilities of a HBO Centre and/or its associated hospital may change, a systematic yearly renewal of the agreement must be provided for. The agreement should include costs for hospitalization and HBO treatment, and must include an obligation to report back to the recognized military HBO expert of the patient's Nation.

5.2 ROUTING

For each military operation where any NATO Nation sends troops, and by extension for each NATO Nation over whose territory possible Medevac of any other NATO Nations' military personnel might take place, it is recommended that evacuation route(s) be established to the selected/appropriate HBO Centers. The responsibility for establishing these routes lies with the Patient Evacuation Coordination Centre (PECC) of each (potential) patient's Nation if such a PECC exists. Alternatively, the coordinating Nation may prospectively establish the shortest (fastest) route and most appropriate transport means from the receiving airfield to the HBO Centre. In Annex C, the current military HBO experts from most European Nations are listed, as a reference. This list needs annual updating.

Other resources available to PECC or equivalent include the following websites:

- www.echm.org
- www.uhms.org
- www.eubs.org
- www.oxynet.org

5.3 PRACTICAL ISSUES TO BE RESOLVED

5.3.1 Evacuation Routing

As availability of civilian and military HBO centres and their associated hospitals may vary in time, no fixed routes can be proposed. For each military operation theatre, these routes need to be prepared and

reconnoitred case by case. However, once a suitable HBO facility has been identified, organizing this routing should, in Western countries, not pose significant problems.

5.3.2 Financial Agreements

Existing financial agreements between NATO Nations' Defence Departments and civilian health care institutions should encompass the emergency HBO care of wounded military personnel, as they would emergency neurosurgery or burn wound care.

The responsibility for these financial agreements should thus be transferred from the Medevac planners to each nation's Defence Department. However, in the process of planning, it is recommended to negotiate a fixed day-price for medical care, including HBO therapy, beforehand. In the current context of civilian health care financing, most civilian hospitals would not oppose such an "a priori" agreement.

5.3.3 Evaluation of Efficacy

As for most of the "accepted HBO indications", the scientific Level Of Evidence (LOE) can still be improved, it is recommended that a systematic data collection be undertaken for each treated case. In cases where no HBO can be administered, ideally the same information should be collected in order to ultimately permit a post-hoc analysis of efficacy of treatment. While this cannot replace a true randomized controlled prospective trial, it is acknowledged that in the specific military context with multi-national – multi-theatre patients, such trials are unrealistic.

5.4 PROPOSAL FOR LECTURE SERIES

5.4.1 Objectives

It is apparent that in almost none of the Western countries, academic medical education in the rationale, the effects and the indications for HBO therapy exist. This implies that, unless specific medical post-graduate training is or has been accomplished, military healthcare personnel (with medical doctors as an example) have had no or very little theoretical knowledge of the possibilities and benefits of HBO therapy for the wounded under their care.

Furthermore, the indications for HBO therapy depend largely on a "cost-benefit" or "risk-benefit" evaluation, and civilian "rules and guidelines" cannot be extrapolated simply to the military operational medical setting.

Therefore, this RTG proposes the setting up and conduction of a Lecture Series, aimed at NATO military medical officers, in order to gain a proper basic knowledge and applicability of HBO therapy in the context outlined above.

5.4.2 Proposal

A STO Lecture Series (LS) is proposed, where in a two day program, essential principles of pathophysiology and therapeutic rationale of HBO therapy will be taught. The LS will be held on three occasions over a two-year period, within the framework and with the support of STO.

Lecturers will be chosen so as not only to be able to provide expert medical knowledge, but also to "make the link" with the specific military situations and "cost/risk-benefit" evaluations encountered in this field.

A certificate of attendance will be issued upon completion of the course – however, the LS in itself does not substitute for proper academic training.

Annex A – SCIENTIFIC BACKGROUND AND RATIONALE FOR THE USE OF HYPERBARIC OXYGEN THERAPY IN DISCUSSED DISEASES AND CONDITIONS

A.1 ACOUSTIC TRAUMA

A.1.1 Pathophysiology of the Condition

Acoustic trauma is defined as injury to the "hearing structures" in the inner ear due to very loud noise.

Damage to the hearing mechanisms may be caused by an explosion near the ear, gunshots, or by long-term exposure to loud noises. Symptoms are hearing loss (usually partial and involving high-pitched sounds) and noises, ringing in the ear (tinnitus). The higher the intensity of the sound, the greater its potential to cause hearing damage. The sound pressure levels capable of causing acoustic trauma vary among individuals on the average around 130 – 140 dB. Single exposures to impulse noises above 140 decibels have the potential to cause permanent damage. A gunner on a 105 mm towed howitzer experiences an impulse noise of 183 dB [1]. A service member who shoots a rifle is exposed to 157 – 163 dB and a gunner with a machine gun, 145 dB. Military men suffering from an improvised explosive device are exposed to impulse noise in excess of 180 dB.

Exposure to noise from firearm use during military service is probably the most frequent etiology of acute acoustic trauma worldwide; it is most commonly regarded as a professional disease in military populations. The hearing loss is sudden, sometimes painful, and is often followed by a (newly) onset of tinnitus. Soldiers sent to battle zones are over 50 times more likely to suffer hearing loss and/or tinnitus than soldiers who do not deploy. As a result of ongoing combat operations, one in three post-deploying soldiers report acute acoustic trauma and one in four reports on hearing loss and/or hearing complaints, including tinnitus.

The number of US service members on disability because of hearing damage is expected to grow up by 18% per year, with disability payments totaling $1.1 billion annually in 2011. Hearing loss is the fourth leading reason for medical referral for combatants routinely returning from their deployments [2]. From more than 5,000 post-deployment soldiers from Iraq and Afghanistan who were referred to audiologists, 1,550 reported exposure to acute acoustic blast trauma. Of those, 72% had resulting hearing loss. Among all post-deploying personnel who received hearing evaluations, 28% have some degree of hearing loss. More than two-thirds of British troops returning from Afghanistan are suffering severe and permanent hearing damage [3].

A.1.2 Rationale for HBO Therapy

A.1.2.1 Theoretical Benefit of HBO Therapy

Direct mechanical injury to the sensory cells of the cochlea is thought to be the main mechanism of injury in acoustic trauma. The cochlear activity is dependent on energy supply which is itself directed by oxygen metabolism [4]. The stria vascularis and the organ of Corti, as well as organs with high metabolic activity, have high oxygen consumption. Arterial oxygen diffuses from the capillary into the inner ear fluids; and increased partial oxygen saturation influences the oxygen tension of the inner ear. The use of Hyperbaric Oxygen Therapy (HBO) has long been proposed as a good way of increasing perilymphatic oxygen pressure: the vastly increased arterial and capillary oxygen tension increases the oxygen tension of the perilymphatic fluid by more than 400% of its initial value, and this state persists for one hour after termination of HBO. This high partial oxygen pressure restores oxygenation to the hypoxic areas of the cochlea and accelerates the biological mechanisms involved in functional recovery. Furthermore, oxygen diffusion from the middle

ear through the round window exerts its rheological effects in the cochlear region independently of haematocrit and blood viscosity.

The rationale in treating acoustic trauma with HBO is not only based on its general effects (massive increase in dissolved oxygen, vasoconstriction leading to oedema reduction, restoration of blood flow, deformability of red blood cells), but also on the potential for specific local effects. HBO may have an effect in restoration of oxidative metabolism in the stria vascularis and in protection of neurosensory cells whose metabolism has slowed down and thus secondarily initiate the recovery of physiological energy metabolism. In improving oxygenation in the inner ear, HBO increases transmembrane potential and ATP synthesis, and activates cell metabolism and the Na+/K+ pump, leading to a restoration of ionic balance and of electrophysiological function in the labyrinth.

A.1.2.2 Animal Experiments

Using animal experiments, it was established that HBO leads to an important increase in the oxygen partial pressure of the perilymph of the guinea pig cochlea [5]. It was shown that 60 hours after damage by acoustic trauma, the number of inner ear sensory cells that had suffered morphological damage in the animal was lower in those treated with HBO than without it. Cochlear blood flow, perilymphatic partial pressure of oxygen, cochlear microphonics, compound action potentials of the auditory nerve, and auditory brainstem responses were studied in noise-exposed guinea pigs during and after the additional treatments [6]. The best therapeutic effect on noise-induced hearing loss was achieved with a combination of HBO and prednisolone. All other therapies were significantly less effective or did not improve noise-induced reduction of auditory evoked potentials. The actual efficiency of the present medical treatments of acoustic trauma of guinea pigs indicated that in some animals the recovery of the threshold shifts are complete despite the fact that significant areas of hair cells are damaged [7]. Results indicated that pure oxygen and carbogen seem ineffective, and corticoids and combined treatment with corticoid/hyperbaric oxygen improve functional and morphological recovery.

After the exposure of Wistar rats to 60 impulses of 162 dB from a 7.62 mm assault rifle, animals were exposed to HBO for 90 min daily for 10 consecutive days at 0.25 MPa [8]. After 4 weeks, auditory brainstem responses were measured and cochleae were processed by light microscopy. The impulse noise caused permanent damage to the cochlea, but a significantly smaller number of hair cells were missing in the HBO group. The morphological damage was also reflected in function, as measured by auditory brainstem responses. Signal-to-noise ratios of rats were significantly decreased after the acoustic trauma [9]. HBO was started at different time after noise exposure. The evaluation on the third day showed that recovery had begun in all groups except the group in which the HBO was started 1 hour after exposure.

The influence of HBO on regeneration processes which take place in the inner ear of chickens after exposure to wide-band noise at the level 120 dB for 48 hours was found [10]. HBO applied once a day after exposure to the noise restricted extent of damage and decreased the dynamics of hair cells injury. The effects of HBO on guinea pigs exposed to noise in the 4 kHz range with intensity of 110 dB sound level pressure for 72 h showed significant difference in the signal-to-noise ratio of the distortion product otoacoustic emission and the scanning electron microscopy findings revealed damaged outer hair cells after exposure to noise, with recovery after HBO [11].

A.1.2.3 Human Data

Victims of acoustic traumata occurring in military service were treated with HBO [12]. A statistically significant amelioration of this hearing-loss was found. The results are more convincing when HBO could be started as soon as possible. The effect of HBO on 122 soldiers suffering from acute acoustic trauma showed that HBO shortened the course of healing with respect to high-pitch perception dysacusis [13]. The results of treatment after an observation period of 6 weeks were also more favourable when patients were treated with

HBO in comparison to patients given only infusions or vasoactive substances. Similarly, the use of HBO also reduces the frequency of relapse following discharge from hospital. In contrast, the vasoactive substance chosen (betahistine) failed to have a favourable effect on the course of healing. No method could be compared with HBO in eliminating tinnitus following acoustic trauma.

Therapeutic results confirmed that 65% of miscellaneous treated patients demonstrated a hearing improvement [14]. In the cases with no hearing improvement, HBO was administered after unsuccessful conventional therapy. If HBO had started from 2 to 6 weeks since acoustic trauma, one half of the cases showed a marked hearing gain, one-third of patients showed a moderate improvement. 4% of patients no longer experienced tinnitus, 81% observed a significant decrease and only 1% an intensity increase of their tinnitus. If HBO was administered at a later stage, but still within 3 months following a trauma, 13% of patients showed a definite improvement in hearing and 25% a moderate improvement. 7% of them no longer suffered from tinnitus, 44% reported an intensity decrease. If HBO was started longer than 3 months up to several years, no hearing improvement was found in the majority of patients; however, one third of the cases reported an intensity decrease of tinnitus. It may be deduced that HBO is recommended and warranted within 3 months after onset of disorder.

Significant difference in audiometry results obtained before and after HBO was noted in 4 kHz when considering all damaging factors that caused acoustic trauma and in 6 kHz only for damage resulting from shooting [15]. 4 days was the mean time interval between acoustic trauma and starting the pharmacological treatment, 7 days was the mean time interval for the HBO commencement. Statistically significant difference was noted in 4, 6, 8 kHz when HBO was started within 5 days since the acoustic trauma. HBO combined with steroids was an effective method of sensorineural hearing loss treatment following acute acoustic trauma.

The average recovery of hearing and cessation of tinnitus was significantly better after HBO than after normobaric oxygen therapy [16]. The recovery from hearing impairment and tinnitus treated with HBO was compared with ears treated with normobaric oxygen. Both were applied daily for 1 – 8 days. The average recovery of hearing both at high and speech frequencies was significantly better and tinnitus persisted less commonly after HBO.

A comparative review of three different treatment regimens in Belgian military personnel suffering from acute acoustic trauma was reported in 2011. Patients were unique in that a baseline audiometry result was available often less than one year old. Depending on the possibility and timing of HBO treatment, patients were treated with high-dose cortisone and piracetam (a rheological agent), either alone (Group 1) , associated with one standard HBO session per day for 10 days (Group 2) or with two HBO sessions and intravenous cortisone therapy (Group 3). Both treatment Groups 2 and 3 showed significantly better hearing gain than when no HBO was associated [17].

There is evidence that the prompt use of HBO in patients, who have lost their hearing suddenly (ISSHL – Idiopathic Sudden Sensorineural Hearing Loss), may reduce the duration and extent of hearing loss. This is the subject of current research [18]. There is a general consensus that the sooner any treatment is started, the better is the prognosis. HBO implies the administration of oxygen under pressures not lower than 0.2 MPa and for durations not less than 60 min [19]. HBO must be seen as part of a therapeutic continuum, without any interruption of the chain of treatment. It cannot be considered as an isolated treatment modality. In accord with the opinion of experts and with the assistance of literature reviewers, the 7th European Consensus Conference on Hyperbaric Medicine has graded HBO in sudden deafness to Level C of evidence (Consensus opinion of experts).

A.2 ARTERIAL GAS EMBOLISM

A.2.1 Pathophysiology of the Condition

Arterial gas embolism, the presence of air or another gas in the arteries, can occur as a result of pulmonary overpressure (usually as a result of uncontrolled ascent, even possible from very shallow depths, as little as 1 meter depth), [20] but also as a result of blast injury (in an out of water) [21], penetrating chest trauma [22], lacerating liver trauma [23], and passive entry of air into wounds that are elevated above the heart level [24]. Intravenous air entry may be asymptomatic unless a Patent Foramen Ovale (PFO) or Atrial Septal Defect (ASD) is present [25] or when massive amounts of air enter the vessels [26], as the lungs act as a very efficient bubble filter [27].

There are several possible mechanisms of injury. Massive venous air embolism may cause an intracardiac "vapour lock" when the right heart chambers are completely filled with gas. Large quantities of gas cause direct arterial occlusion. However, animal studies have shown that even if no vessel occlusion existed, bubbles cause a progressive decline in cerebral blood flow [28], by neutrophil activation subsequent to endothelial damage by the bubble. In many cases of cerebral gas embolism there is clinical improvement after the initial symptoms, followed by a delayed deterioration a few hours later [29].

Venous gas embolism manifests as hypotension, tachypnea, hypocapnia, pulmonary oedema or cardiac arrest. Arterial gas embolism presents as brutal loss of consciousness, confusion, focal neurological deficits, cardiac arrhythmias or ischemia (due to coronary embolisation of gas). The diagnosis is mainly clinical, with possible evidence of intravascular gas using ultrasound or by direct venous aspiration of gas. Brain imaging, even in the presence of severe neurological abnormalities, may be demonstrating no gas in the cerebral vessels, as these gas bubbles are usually quickly fragmented by the pulse waves and the reactive hypertension [30].

A.2.2 Theoretical Benefit of HBO

Application of hyperbaric pressure reduces the volume of the gas embolus (Boyle's Law); it enables gas removal by denitrogenation (effect of the hyperoxygenation) [31]; it maintains oxygenation in the ischemic tissues and it decreases intracranial pressure and cerebral oedema formation [32].

A.2.3 Clinical Scientific Evidence

Recompression treatment with oxygen has been considered the standard of care since the early 1960's [33],[34]. Human randomised prospective trials obviously are lacking, although retrospective reviews have been conducted, revealing significantly better outcomes with the use of recompression treatment versus non-recompression therapy only [35],[36],[37],[38]. Retrospective data published in 1964 showed a decrease in mortality from 93% with no treatment to 33% with conventional aggressive treatment (left lateral decubitus position, vasopressors, and oxygen by positive pressure). A later study showed a mortality rate of only 7% in 30 patients treated when hyperbaric oxygen was utilized [39]. Animal studies document the superiority of HBO above conventional treatment [40],[42].

As the pathophysiology of the condition involves tissue ischemia, treatment should be started as soon as possible after the clinical diagnosis has been made [44]. However, hyperbaric oxygen therapy has been reported successful in persistent symptoms even after a significant delay [36]. HBO therapy is indicated even if the patient appears to have recovered completely, because of the risk of secondary deterioration [29].

Repeat hyperbaric treatment, usually two or three but occasionally up to 10 sessions, can be performed as long as there is stepwise improvement after each session [43]. As patients can be hemodynamically highly unstable, appropriate medical intensive care and monitoring is mandatory [36],[45]. Adjunctive therapies

include adequate fluid management (in case of concomitant decompression sickness there may be significant hemoconcentration), along with possibly lidocaine [40],[41], NSAID and Low-Molecular Weight Heparin in case of immobilisation for more than 24 hours [46].

A.3 BURN INJURY – LIFE-THREATENING (HIGH TBSA OR RESPIRATORY BURNS)

See Section A.4.

A.4 BURN INJURY – NON-LIFE-THREATENING

A.4.1 Introduction

When soft tissues (such as skin and muscle) are damaged by burning, the blood flow in the damaged area is sharply reduced. This causes an area of swelling which radiates away from the area of damage, in all directions. The swelling may extend deep into muscles, and over the surrounding skin, and cause more damage than the initial injury.

HBO can help to reduce this swelling. The extra oxygen slows down the leak of fluid out of the damaged blood vessels. It also reaches tissues in the damaged area, allowing them to recover. The extent of tissue removal, and the need for amputation, is therefore reduced. In order to work, however, HBO must be used as early as possible.

A.4.2 Pathophysiology of the Condition

Thermal energy transfer to cutaneous cells cause cell and tissue destruction by direct coagulation and cell lysis. In the area surrounding the burn injury, interstitial oedema occurs, causing a microvascular compromise, with red blood cell sludging and finally capillary stasis [84]. The maximum of this microvascular compromise has been shown to occur within 24 hours [54],[55],[56].

Tissular hypoxia and ischemia occurs as a result of this stasis [82], which increase oedema by loss of integrity of the capillary wall (endothelial cell contraction). This fluid loss, by changing the oncotic pressure gradient across the capillary vessel wall, further decreases the intracapillary fluid pressure and thus increases stasis [57],[58],[59].

As a result, areas of burnt tissue that were initially second degree (partial thickness burn), are observed to progress within the first 24 hours after the burn, into deep second degree or third degree (full thickness) burns, needing early excision and grafting in order to heal. This happens even with optimal fluid resuscitation protocols [50],[53].

The tissue lesion caused by thermal energy induces a massive inflammatory reaction, with leucocyte stimulation, margination and activation. The resultant production of oxygen free radicals is further enhanced in the second (reperfusion) stage of the burn wound evolution [83]. This phenomenon is partly responsible for the generalized inflammatory reactions occurring in the bowel and lungs of severely burnt patients. This may lead to multi-organ failure and semi-delayed death [63],[64],[65],[66].

The third cause of death in burn patients is related to systemic infection during their hospital stay. Not only is there a large possible port of entry by loss of the epithelial barrier, also the immunologic state of a severely burnt patient is depressed, making him/her much more susceptible to infections [60],[61],[62],[90].

The mainstay of treatment of deep partial thickness or full thickness burns is the excision of the affected skin and coverage with a temporary (cadaver skin, synthetic skin equivalent) or permanent (autograft) epithelial

layer [48],[49]. In order for such a skin graft to "take" the underlying wound bed must be well perfused and "healthy". In cases where the oxygenation of the avascular skin graft cannot be ensured by diffusion of underlying wound bed (either by insufficient vascularisation or by utilisation of molecular oxygen by infectious microorganisms) the skin graft will fail, necessitating a renewed surgical intervention, possibly after a delay of approximately 10 – 14 days, needed for healing of the donor site. This increases the risk of infection and systemic complications [47],[51].

In all of these pathophysiological mechanisms, hypoxia plays a pivotal role. Oxygenation of ischemic tissues must be done in a rapid and massive way, in order to decrease paradoxical tissue damage by ischemia-reperfusion phenomena. Hyperbaric oxygenation is the only therapeutic means capable of ensuring this [98],[99].

A.4.3 Theoretical Benefit of HBO

A.4.3.1 In Vitro Studies

Antibacterial effect:

- Oxygen pressures as high as 200 mmHg have been shown to effectively inhibit growth and proliferation of anaerobic and facultative aerobic bacteria [86].
- A synergistic effect of oxygen and antibiotics has been demonstrated for clindamycin, aminoglycosids, amoxycillin/clavulanate and quinolones; this effect is not apparent for metronidazol, an antibiotic specifically developed for anaerobic infections [87].
- The bactericidal activity of polynuclear leukocytes is severely impaired in case of low surrounding oxygen tensions, limiting the capacity for "oxidative burst" of those cells. In fact, it has been shown that at "normal" tissue tensions of 40 – 50 mmHg, polynuclear leukocytes only function at half-maximal oxidant killing capacity, and that this capacity is maximal at around 300 mmHg [88],[89].

A.4.3.2 In Vivo (Animal – Human)

A.4.3.2.1 Fluid Loss

In a canine burn model of 40% TBSA, a reduction of the plasma loss of about 40% has been observed when HBO was administered in the early phase after injury (3.0 ATA, twice daily) [68]. A similar effect has been observed in a human – prospective, randomized – study, illustrating not only the pre-capillary vasoconstriction induced by HBO but even more importantly, the preservation of the integrity of the capillary vessel wall: in the first 24 hours after the burn, HBO-treated patients needed an average volume resuscitation of 2.2 ml/kg per %TBSA, whereas the control group needed 3.4 ml/kg % – a reduction of 35% [69]. A retrospective human study of 21 patients, of which 10 received HBO (2.0 ATA, 90 minutes, twice daily) in the acute phase, confirmed this reduction in necessary perfusion volumes [70].

A.4.3.2.2 Preservation of Dermal Elements [72],[76],[79]

In study in 1996, a "deep partial thickness" burn of 5% TBSA was created in rats which progressed, in a reproducible way, towards "full thickness" after 24 hours. Comparing two groups of animals, one who received a "classic" burn treatment and the other who received the same treatment plus two sessions of HBO (2.0 ATA, 60 minutes) per day, a preservation of deep dermal elements was observed, classifying the burn still as "second degree" at day 5 in the HBO-treated animals [73]. Very recently, a similar study report was published, confirming the effects of HBO on the preservation of regeneratory active follicles ($p = 0.009$) and on the rapidity of epithelial regeneration ($p = 0.048$) [74].

A.4.3.2.3 Antibacterial Effects

The antibacterial effects of HBO which have been known by its use in other pathologies have been confirmed in an animal burn wound model, even though its effect was less than that of silver sulfadiazine [75],[85]. This is not surprising, since molecular oxygen does not have a direct antibacterial effect at the pressures obtained in tissues under HBO. However, HBO restores the oxido-reduction potential in the (burned) tissues, thereby maintaining the leukocyte killing capacity of PMN and preserving the natural resistance against infection [102],[103].

A.4.3.2.4 Reduction of Ischemia-Reperfusion Effects

Several animal studies have demonstrated the reduction of inflammatory (leukocyte) infiltration in the burnt tissues as well as in distant tissues (lung and bowel) [96].

Oxidative damage has been evaluated in HBO-treated animals compared to classically treated animals, showing a reduction in free radical end products, TNFa and complement activation. In humans, this has been further confirmed with a reduction in soluble IL-2 receptor and preservation of fibronectin in burn patients [100].

Considerable attention has been given to the use of HBO in inhalation injury. There is currently a fear that it may cause worsening of pulmonary damage, particularly in those patients maintained on high levels of inspired O_2 [52]. Grim and colleagues from the University of Chicago Burn Center [101] reported no evidence of oxidative stress in HBO treated burn patients, using exhaled products of lipid peroxidation as a marker. Ray and colleagues [110] have analyzed serious burns being treated for concurrent inhalation injury, thermal injury, and adult respiratory distress syndrome, and noted no deleterious effect in those patients on continuously high-inspired oxygen. More rapid weaning from the ventilator was possible in the HBO treated group ($p < 0.05$). A significant savings in cost of care was achieved through the use of hyperbaric oxygen in this study ($p < 0.05$). There is presently no evidence to controvert these data [104],[105].

A.4.4 Clinical Scientific Evidence

Although a number of very convincing prospective and retrospective studies have been published [80],[81],[94],[95], demonstrating a reduced need for surgical interventions, a reduced mortality, a reduced duration of hospital stay, and reduced cost of treatment when systematically using HBO therapy adjunctive to classical therapy, to date no randomized controlled prospective, placebo-controlled trial has been published to unequivocally prove the effect of HBO therapy [77],[78],[106],[107]. Therefore, the acceptance of HBO as a valuable adjunctive treatment remains limited to those burn centers that are capable of providing early, intensive care HBO treatments, without adding supplementary (infectious, hemodynamic) risks to the patient's condition [67],[71],[108].

Over the past 20 years, the pendulum swung to an aggressive surgical management of the burn wound, i.e. tangential excision and early grafting of the deep second-degree, probable third-degree burns, especially to functionally important parts of the body. Hyperbaric oxygen, as adjunctive therapy, offers the surgeon yet another modality of treatment for these deep second-degree burns to the hands and fingers, face and ears, and other areas where the surgical technique of excision and coverage is often imprecise. These wounds, not obvious third degree, are then best treated with topical antimicrobial agents, bedside debridement, and adjunctive HBO, allowing the surgeon more time for healing to take place and to better define the extent and depth of injury. Adjunctive HBO can drastically reduce the healing time in the major burn injury, especially if the wounds are deep second degree [91],[92],[93],[94],[95].

There is some theoretical benefit of hyperbaric oxygen therapy for obviously less well-defined third-degree burns. Fourth-degree burns, most commonly seen in high voltage electrical injuries, benefit from several

processes, including reduced fascial compartmental pressures, reduced swelling of injured muscle due to preservation of aerobic glycolysis, and greatly reduced anaerobic infection.

Finally, reconstruction utilizing flaps and composite grafts, e.g. ear to nose grafts, can be greatly facilitated with HBO [97]. Often the decision to use HBO will be made intraoperatively because a surgeon is concerned about a compromised cutaneous or musculocutaneous flap.

In summary, HBO should be used in life-threatening burn injuries only when it can be applied early and aggressively, in order to limit the secondary tissue destruction caused by the thermal injury and its consequences.

In non-life-threatening burn injuries, especially to "difficult" areas such as ears, nose, hand, perineum, HBO should also be applied early in order to limit the early debridements and progressive tissue destruction [111].

A.5 CARBON MONOXIDE POISONING

A.5.1 Introduction

Carbon monoxide (CO) is a colorless, odorless and tasteless gas produced by the incomplete combustion of carbon-based compounds. While the heme catabolism is an endogenous source of CO, most frequent exogenous sources are house fires, poorly functioning heaters, chimneys, gas–powered electrical generators, automobile and cigarette smoke. Several occupational groups such as fire fighters and miners tend to be most at risk for CO poisoning. Some age groups and particular conditions such as the elderly, unborn babies, infants, children and pregnant women are also more susceptible to poisoning [112],[113]. Additionally, individuals with chronic heart disease or respiratory insufficiency and patients with decreased oxygen-carrying capacity (i.e. anemia, blood cancer) are more prone to suffer severe poisoning.

Cardiac and brain tissues are the most vulnerable tissues in CO poisoning [114]. Signs and symptoms associated with cardiotoxicity or brain injury are usually observed in the severely poisoned patient. While cardiotoxicity is usually responsible for acute death, brain injury is mostly responsible for delayed signs and symptoms. Pathologies implicated with cardiotoxicity are tissue hypoxia causing cellular damage, CO binding to cytochrome-c oxidase leading to impaired cellular metabolism, ROS mediated lipid peroxidation and cellular death. CO induced cardiotoxicity causes decreased myocardial function (pump failure) due to myocardial ischemia. Additionally, CO cardiotoxicity may lead to several cardiac rhythm abnormalities [115]. The central nervous system is particularly sensitive to the toxic effects of CO poisoning. While petechial hemorrhage associated with severe CO poisoning may cause death in the acute phase, brain edema accounts for the majority of CO related deaths in the sub-acute phase. The most common clinical scenario affecting the central nervous system in CO poisoning, however, is Delayed Neurologic Sequelae (DNS). CO poisoning may cause demyelination of the nerves and may lead to necrosis of the globus pallidus, susbstantia nigra, thalamus or putamen, namely the basal ganglia [116]. The more severe the acute state the higher the risk of DNS development. Neurological deterioration may occur over a wide span of time, but commonly occurs within 2 to 40 days. The prevalence varies from 1 to 47%. Older people are more susceptible. While complete resolution usually occurs within 2 months in patients with mild CO poisoning, it may take up to one year in patients with severe poisoning [117].

A.5.2 Pathophysiology of the Condition

There are 3 main pathways implicated with carbon monoxide poisoning:

- Hypoxia;

- Perivascular injury; and
- Excitotoxicity.

A.5.2.1 Hypoxia

CO rapidly binds to hemoglobin and forms carboxyhemoglobin (CO-Hb). Compared with oxygen, CO binds to hemoglobin with a 200 fold higher affinity. As the level of CO-Hb increases the oxygen hemoglobin dissociation curve shifts to the left and increases its affinity for oxygen ultimately causing tissue hypoxia. CO causes hypoxia through several mechanisms, as detailed in the sub-sections below.

A.5.2.1.1 Anemic Hypoxia

Anemic hypoxia is the earliest and most frequent consequence of CO poisoning. Following the binding of CO, hemoglobins are almost non-functional and can neither bind nor release oxygen. Although this condition is termed as anemic hypoxia, it significantly differs in that in carbon monoxide poisoning, in contrast to anemia, the oxygen dissociation curve displays a leftward shift and therefore the affinity of hemoglobin for oxygen is increased, further limiting oxygen delivery to the tissues.

A.5.2.1.2 Histotoxic Hypoxia

Carbon monoxide does not merely bind to hemoglobin but also to a critical enzyme functioning normally in the electron transport chain, i.e. cytochrome a,a3 enzyme. This binding incapacitates oxidative phosphorylation and thereby deprives body systems of their energy source.

A.5.2.1.3 Oligemic Hypoxia

Oligemic hypoxia occurs due to the binding of carbon monoxide to myoglobin. The resulting non-functioning compound is termed as carboxymyoglobin (Mb-CO). Mb-CO is, in great part, responsible for carbon monoxide induced cardiotoxicity. Severe poisoning with Mb-CO may cause ischemic myocardial damage and impair cardiac output thereby leading to oligemic hypoxia. Additionally arrhythmias are frequently observed in patients with Mb-CO induced cardiotoxicity.

A.5.2.2 Perivascular Injury

CO binds to the heme proteins in platelets. This binding activates platelets, which release Nitric Oxide (NO) to plasma [118]. NO reacts with neutrophil derived superoxide and form the peroxynitrite ($ONOO^-$) molecule, which is a potent nitrating and oxidizing agent. Peroxynitrite activates platelet adhesion molecules and causes platelet-neutrophil aggregation [119]. Neutrophil interaction with platelets or with the endothelium is a strong stimulus for degranulation. While primary granules of neutrophils comprise several deleterious enzymes such as elastase, Myeloperoxidase (MPO) and lipase, secondary or tertiary granules involve metalloproteinases and ß2 integrins. MPO release promotes endothelial oxidative stress and induces the synthesis of adhesion molecules for neutrophils, which lead to additional neutrophil aggregation. Neutrophil-derived proteases react with Xanthine Dehydrogenase (XDH) to form Xanthine Oxidase (XO), which is the major source of Reactive Oxygen Species (ROS), particularly superoxide, in the sub-acute phase.

A.5.2.3 Excitotoxicity

CO poisoning causes neutrophil diapedesis and brain lipid peroxidation by activating neutrophils [120]. Endogenous protective mechanisms against oxidative stress are impaired due to XO activation and lipid peroxidation occurs within the brain tissue. Lipid peroxidation products such as malondialdehyde interact

with Myelin Basic Protein (MBP) and change its three-dimensional structure and stimulate lymphatic immune reaction, which in turn induces microglia expression and activation, eventually starting an inflammatory process. Lipid peroxidation products cause injury to neural membranes and are believed to be responsible for neurologic symptoms and sequelae.

Glutamate is an important neurotransmitter implicated with neural toxicity [121]. Glutamate induces N-Methyl D Aspartate (NMDA) activation and Ca^{+2} influx into the cell cytoplasm. Ca^{+2} activates several deleterious enzymes such as protease, phospholipase and endonuclease, which together cause cellular membrane damage and DNA injury.

A.5.3 Theoretical Benefit of HBO

While the half-life of oxygen is around 320 minutes in room air (21% oxygen), it is approximately 60 minutes while inspiring 100% oxygen from a non-rebreather mask and only about 23 minutes while inspiring 100% oxygen inside a hyperbaric chamber at 3 atm abs. The effects of HBO on hypoxia associated with CO poisoning is well established.

Given the fact that lipid peroxidation is an important aspect of CO-induced neurological injury, the inhibition of Beta-2 integrins on the cell surfaces of neutrophils by HBO treatment is recognized as a significant benefit of HBO treatment. HBO treatment at 3.0 atm abs has been shown to prevent the adherence of neutrophils to the endothelium and thereby blocked leukocyte-mediated inflammatory changes and alleviated Reactive Oxygen Species (ROS)-related oxidative stress [124].

CO binds to the cytochrome a,a3 enzyme of the electron transport chain in the outer membrane of the mitochondria and impairs electron transport, thus oxidative phosphorylation and ATP production. This causes histotoxic hypoxia as well as an increase in ROS formation. HBO has been shown to improve mitochondrial function and increase adenosine triphosphate production [122].

Last, but not least, HBO resolves cerebral edema through vasoconstriction [123]. Indeed, HBO treatment is unique in increasing oxygenation while causing vasoconstriction.

A.5.4 Literature

Experimental studies have shown that in addition to resolving tissue hypoxia, HBO treatment restores mitochondrial oxidative metabolism [122] prevents lipid peroxidation [124] and impedes leukocyte-endothelium adhesion [125].

The majority of clinical studies with HBO have demonstrated favorable outcomes as compared to treatment protocols without HBO. Weaver et al. in a randomized, double-blinded, placebo-controlled study conducted on 152 patients, administered either HBO or normobaric oxygen to patients with CO poisoning. Almost half of the patients had a history of loss of consciousness 8% of whom were intubated. Of note, patients in the HBO group received 3 sessions within 24 h of which the first comprised treatment at 3.0 atm abs pressure for 50 min and treatment at 2.0 atm abs for 60 min, followed by two additional sessions at 2.0 atm abs for 90 min oxygen breathing, each. At 6-weeks follow-up, neurologic examinations revealed that 25% of patients who received HBO versus 46.1% who did not had still signs of neurologic sequelae [odds ratio: 0.39; 95% CI 0.20 to 0.78] [117].

In another randomized controlled study, 65 patients with CO poisoning received either HBO or normobaric oxygen. Patients with a history of loss of consciousness were excluded and hence the study assessed merely patients with mild to moderate CO poisoning. Patients in the HBO group received only 1 HBO session with a maximum pressure at 2.8 atm abs. While none of the HBO treated patients experienced neurologic sequelae at follow-up, 23% of those who did not receive HBO suffered various symptoms related to neurologic deterioration [126] .

Gorman et al. [127] in a non-randomized longitudinal study reported their results from 100 patients with CO poisoning. Of these 8 received normobaric oxygen alone, 24 one HBO session and 68 two or more HBO sessions. At study completion data analysis revealed that while patients who received NBO or a single HBO displayed similar rates of neurologic sequelae at both discharge (63 and 46 %) and one month follow-up (67 and 50 %); a significantly lower rate of neurologic sequelae, at discharge and one month follow-up, was observed in patients who received 2 or more HBO sessions (13 and 18 %, respectively).

In contrast to these trials, several others failed to demonstrate a benefit of HBO in CO poisoning. Rapahel et al. [128] in an unblinded study randomized a total of 343 patients to receive either NBO or 1 session of HBO administered at 2.0 atm abs. None of the patients had a history of loss of consciousness. Outcome results assessed at one month follow-up revealed similar rates of persisting neurologic symptoms (32.1% vs. 33.8%, respectively) for both groups. Patients received additional HBO sessions, up to 6, until neurological recovery.

Scheinkestel et al. [129] enrolled a total of 191 patients, 73% of whom suffered severe CO poisoning, and almost half were comatose. Patients were randomly assigned into either HBO or sham HBO groups and received continuous oxygen by face mask for 3 days between the sessions. Outcomes were assessed at completion of study and at one month follow-up. While 74% of the patients in the HBO group displayed persistent neurologic sequelae at treatment completion, 68% in the sham HBO group displayed similar symptoms. Unfortunately a large number of the patients were lost to follow-up at 1 month (54%), rendering reported results controversial. Nonetheless, study results revealed similar outcomes for each treatment arms at one month follow-up. This study was criticized on the basis that patients in the control arm received high oxygen doses and hence results could not be generalized.

Annane et al. [130] recently conducted two randomized single blind controlled trials. While the first trial included 179 patients who suffered a transient loss of consciousness (malaise, syncope) the second included 206 patients with coma. In the first trial patients were treated with 6 h of NBO or with 4 h of NBO plus one HBO session. In the second, patients received either 4 h of NBO plus one or two HBO sessions. Of note HBO sessions were administered at 2 atm abs. In summary, the authors failed to demonstrate a significant benefit of one session HBO therapy over NBO therapy in patients with transient loss of consciousness. Similarly, two sessions of HBO therapy did not yield any benefit over one HBO session in comatose patients.

A.6 CRUSH INJURY (COMBINED TRAUMA TO BONES, SOFT TISSUE, VESSELS, OR NERVES)

A.6.1 Pathophysiology

The term crush injury summarizes traumatic vascular injuries that cause severe tissue damage and make tissue survival questionable. The injuries result in local hypoxia (and possible systemic effects, e.g. shock).

Ischemia leads to edema and vice versa. Ischemia is caused by direct vascular trauma, fluid leakage or compartment syndrome. All these changes lead to tissue hypoxia.

Edema is either vasogenic or cytogenic and it enhances the diffusion distance from oxygen to the cells. Edema also leads to capillary collapse and thus extends the degree of hypoxia.

If reperfusion can be established this leads to excessive production of oxygen radicals that cause vasoconstriction and finally even more hypoxia [159],[170].

Table A-1: Patient Assessment and Recommendations for HBO.

Patient Assessment (from Kindwall, pp. 508-509) [152]				
Factors	**Scoring Criteria (0 → 10 scale)**			**Comments**
	2 points	1 point	0 points	
Age	< 40 yrs	40 – 60 yrs	> 60 yrs	1) Use ½ points when the severity of involvement is between two scoring criteria. 2) For ambulation scoring criteria subtract ½ point if walking aids (e.g. walkerette or crutches) are required. 3) Where two factors such as 'smoking/steroid use' are listed, use the scoring criteria, which reflects the more severe involvement.
Ambulation	Community	Household	None	
Smoking / Steroid Use	None	Over 5 years ago	Current	
Cardiac / Renal	Normal	Compensated with medications	Decompensated even with medications	
Neuropathy / Deformity	None	Mild-to-moderate	Severe	

Recommendations for HBO after patient assessment		
Score	**Severity of Compromise**	**HBO Indication**
8 – 10	Normal Host	No
4 – 7	Impaired Host	Yes
3 or Less	Severely Compromised Host	Yes

Clinical stages: the most used classification for crush injury is the Gustilo classification [143].

Table A-2: Gustilo Classification and Recommendations for HBO.

Use of HBO for Open Fractures – Crush Injuries (Gustilo Classification)					
Type	**Mechanism**	**Expected Outcome**	**Use of HBO and Host Status (see Table A-1)**		
			Normal Host (score 8 – 10)	Impaired Host (score 4 – 7)	Severely Compromised Host (score 3 or less)
I	Small (< 1 cm) laceration from inside to outside	Usually no different from a closed fracture	No	No	Yes
II	Large laceration, but minimal soft tissue damage	Usually no different from a closed fracture	No	Yes	Yes
III	Crush Injuries				
	a) Sufficient soft tissue to close wound (primary or delayed)	Infections and/or nonunion rates < 10%	No	Yes	Yes

Use of HBO for Open Fractures – Crush Injuries (Gustilo Classification)					
Type	**Mechanism**	**Expected Outcome**	**Use of HBO and Host Status (see Table A-1)**		
	b) Flaps or grafts required to obtain soft tissue coverage	About 50% incidence of complications (infections, nonunion)	Yes	Yes	Yes*
	c) Major (macrovascular) vessel injury	About 50% incidence of complications (infections, nonunion)	Yes	Yes	Yes*
* Consider primary amputation with adjunctive HBO for wound healing and flap survival.					

A.6.2 Theoretical Benefit of HBO

The main goal of hyperbaric oxygenation in crush injuries is to establish tissue hyperoxygenation. When pressurized to more than 2,4 bar almost all oxygen becomes dissolved in plasma, thus tissue cells could remain alive without any other oxygen carriers (reduced hemoglobin and/or reduced perfusion) [133].

Secondly, an important effect of HBO is vasoconstriction, which leads to significant **reduction of edema** (more than 20%).

Third, hyperoxygenation improves the anti-bacterial action of neutrophils and is inhibitory to anaerobic microorganisms [160].

Fourth, HBO protects from **reperfusion** injuries due to the antagonism of lipid peroxidation and other cellular or humoral reactions [170].

Fifth, HBO improves the work of fibroblasts, some authors postulate a promotion of neurogenesis or even angiogenesis due to HBO. It may improve the outcome of skin grafts.

A.6.2.1 In Vivo

Animal models (rodents, dogs) of crush injury studies have shown significant effects of HBO therapy: reduction of muscle necrosis, improved wound healing, fewer amputations, improvement of osteogenesis, improvement of microvascular blood flow, less muscular edema and better neutrophil adherence to vascular walls. It has no effect on myogenic transcription factors [132].

A.6.2.2 In Vitro

HBO also regulates inflammatory gene expression in endothelial cells and can lead to decrease in apoptosis expression.

A.6.3 Clinical Scientific Evidence

A Medline search was performed for the items “HBO and crush injury” back until 1969. There are well-established animal models of crush injury; however data on human casualties are rare. There only 28 hits for both items (HBO and crush injury) in Medline. Most of the data result from case reports or series of up to 35 patients. There is only one RCT that compares crush injuries with and without HBO therapy [134], where HBO improved healing and reduced surgical procedures significantly. Especially patients over 40 profited from HBO treatment.

Several clinical scales have been proposed to select patients suitable for HBO treatment. The items included age, limb ischemia, shock, skeletal and soft tissue injury.

For best results on human crush injuries the following recommendations exist:

- Gustilo grades IIIb and IIIc;
- HBO should be administered "as soon as possible";
- If surgery is delayed for more than one hour, HBO could/should be administered first; and
- 3 – 4 HBO sessions/day for 3 days, then 2 sessions/day for 2 days, 1 session/day for 3 more days [139],[152].

Management is two-fold:

- Firstly, direct interventions are required (surgical); and
- Secondly, management of all indirect effects of the injury (fluid replacement, antibiotics, adequate oxygenation) is needed.

Data are rare, levels of evidence are low ("Expert Opinion"). There is an obvious need for more studies [141]. From the existing data the experts conclude that the adjunctive use of HBO in crush injuries may result in a favorable outcome for selected patients [139],[141].

A.7 DECOMPRESSION SICKNESS – LIFE-THREATENING

See Section A.8.

A.8 DECOMPRESSION SICKNESS – NON-LIFE-THREATENING

A.8.1 Introduction

Decompression Sickness (DCS) is a clinical entity caused by the rapid desaturation of tissues due to a reduction in surrounding (atmospheric) pressure. The formation of inert gas bubbles in tissues and or in the blood stream causes mechanical damage (compression of tissue structures) and biochemical effects by the inflammatory responses between the blood – tissue fluids and the gas phase interface. This may cause pain or organ dysfunction which is essentially ischemic in nature [172]. Usually, symptoms arise within 24 hours after the pressure reduction – this may be after surfacing from a dive or after rapid pressure reduction while at altitude (e.g. loss of pressurisation in an aircraft). Cases have been described of DCS after repetitive deep breath-hold diving, but usually, DCS only arises when compressed gas has been breathed while at depth.

In underwater diving, decompression procedures have been developed since over a century ago [173], designed to allow divers to exit the water after a dive as quickly as possible with low risk of developing symptoms of DCS. However, these "dive tables" were calculated on the basis of a number of theoretical assumptions, derived from animal experiments, and are thus not completely physiologically accurate. Although they have been refined over the years, allowing more flexibility while maintaining a similar safety profile, it is generally accepted that they have a "failure rate" of approximately 0.5%. This of course depends not only on the actual profile of the dive, but also on the time and depth of the previous dive(s) as desaturation is not complete upon surfacing and residual inert gas is present in the tissues for as long as 12 hours after the dive. Decompression obligation calculations for repetitive dives and multi-day diving are less reliable than those for a single dive, and incidences as high as 1/1000 have been recorded in a cohort of live-aboard dive instructors [174].

Symptoms of DCS depend on the territory where decompression gas bubbles are lodged. They are typically classified as "mild" or "Type I" DCS – joint pains, cutaneous rashes, lymphatic obstruction, general fatigue; and "serious" or "Type II" DCS – neurological dysfunction (paralysis, paresthesias, bladder dysfunction), inner ear symptoms (vertigo, hearing loss), cardiorespiratory symptoms (the "chokes") and shock [175].

A.8.2 Theoretical Benefit of HBO

Emergency first aid of DCS consists of general cardiorespiratory support, with adequate fluid resuscitation, as well as the administration of 100% oxygen. In some cases, especially mild or equivocal DCS, and in altitude induced DCS, this may be sufficient and constitute the definite treatment [176],[177].

A return to increased pressure has been observed to alleviate the symptoms of DCS and has been used as a treatment since the mid-19th century. However, recompression with pure oxygen breathing has only been advocated since 1937 [178]. Whereas initially, recompression depth was considered the most important factor, and oxygen use was limited by its toxicity at the commonly used pressures, in 1965 lower pressure, pure oxygen tables were proposed that have been since considered the most efficient treatment for the majority of cases [179].

Hyperbaric oxygen treatment of DCS is now considered the standard of care [180]. A rapid return to elevated atmospheric pressure not only reduces the size of gas bubbles in the body, but the high partial pressure of oxygen increases desaturation and nitrogen wash-out, increases the oxygen diffusion in the tissues and thus reduces the ischemic effects of trapped gas emboli. It is likely that other effects of hyperbaric oxygen therapy play a role in the therapeutic effects, such as a reduction of oedema and of neutrophil adhesion to the capillary endothelium with subsequent extravasation and inflammation [181].

A.8.3 Scientific Evidence

Whereas animal experiments confirm that rapid recompression with oxygen results in prompt cure of DCS, it is by no means easy to extrapolate animal data to humans, as no single animal has been proven to be a perfect model. In humans, no prospective, randomised studies have been performed to compare recompression with expectant management; however, non-randomised outcome studies comparing the "historical" US Navy recompression treatment tables (the US Navy Recompression Tables 3 and 4) tested and recommended since 1945 with "minimal pressure oxygen-breathing" tables in 1965 showed a reduction in failure rate of over 50% [179]. Epidemiological data indicate, as expected, that early hyperbaric treatment yield more likely a complete resolution of symptoms [182],[183]. Current recommendations indicate that, unless recompression can be done within a few minutes, a time frame within 6 hours yields is a reasonable objective [182],[187],[188]. Current data have not established a maximum time after which recompression would be ineffective [184],[185],[186]. US Navy oxygen recompression tables (and similar Royal Navy – UK and Comex – FR tables) are most widely used and have achieved a high degree of success in the treatment of DCS [189],[190],[191],[192]. Higher pressure mixed-gas tables (such as the Comex 30 Heliox treatment table) present some theoretical and (animal-)experimental benefits over oxygen-only tables [193],[194], but necessitate more complex logistics and are thus reserved for facilities and personnel with the appropriate experience, expertise and hardware [195].

Repetitive treatments may be necessary in divers who do not respond satisfactorily to a single hyperbaric recompression treatment, although the efficacy of more than 5 – 10 additional (typically shorter, classical HBO treatments) has not been documented statistically in large series [196].

Adjunctive treatments, except for adequate fluid resuscitation and prophylaxis of venous thrombo-embolism for patients with leg immobility, have not been proven substantially contributing to a better outcome [197],[198],[199].

A.9 FROSTBITE

A.9.1 Introduction

Like thermal burns, frostbite has a profound impact on the local microcirculation. It can be defined either as a hyper-acute cold injury or a prolonged exposure. It has been shown that after thawing, a protracted injury phase occurs, which bears striking resemblance to ischemia-reperfusion injury as has been seen in thermal burns. Theoretically at least, hyperbaric oxygen therapy could represent the following benefits in frostbite injury:

- Reduction of secondary cell death and tissue damage by reducing ischemia-reperfusion injury;
- Early demarcation of viable versus non-viable tissue, allowing for early definite surgical intervention and more rapid rehabilitation; and
- Prevention of secondary infection of vulnerable frostbitten tissues.

These potential benefits of HBO are not unique to frostbite or burns, in fact, most acute traumatic peripheral ischemia injuries (crush, compartment syndrome, flaps and grafts, re-implantations) share pathophysiological elements with these two.

A.9.2 Literature Review

The first case report of the use of HBO in frostbite dates back from 1963 [200], but in the period 1963 – 1974, only 14 more cases have been reported in the literature. Some animal experiments were performed between 1968 and 1972, but since then, no more cases were reported until 2001 [201],[202].

Okuboye et al. [203] demonstrated in the rabbit model (rabbit foot, slow freezing in ethylene bath, rapid thawing) that the use of HBO (3.0 ATA) could reduce tissue loss from 75% in control animals to 25%. On the other hand, Gage et al., [204] using a rapid freezing model to -30°C, also in the rabbit's foot, with active and passive rewarming, could show no effect from HBO. A similarly very cold (-30°C) mouse model (Hardenbergh, 1972), demonstrated a limited benefit of HBO [205].

These differing results indicate that rapid, profound freezing injury may represent some important differences in pathogenesis and tissue injury from slow, moderately cold freezing. In fact, frostbite probably comprises a range of tissue injury from Freezing Cold Injury (FCI) to Non-Freezing Cold Injury (NFCI) to normal but cold tissue. Based on these animal data, HBO would probably only be of use in NFCI.

These animal experiments used early application of HBO, during or immediately after rewarming. Some scattered case reports seem to hint that even a long time after rewarming, HBO may be of some benefit – although, since these are uncontrolled and single reports, the evidence backing these claims is not very strong. In 2001, von Heimburg reported on a case where HBO was only applied after 4 days in a young boy whose both hands were frozen, saving all fingers [206]. Similarly, cases were reported 12 and 22 days after cold injury, where the microcirculation clinically improved dramatically after application of HBO, and this treatment was considered a key factor in the preservation of all toes and fingers [207],[208].

A.9.3 Mechanism of Action of HBO

Based on these animal experiments and human case reports, elements of beneficial action can be defined in all stadia of the injury and recovery:

- Tissue survival (capillary stasis);
- Oedema reduction;
- Infection prevention;

- Necrotic tissue demarcation; and
- Faster granulation and epithelialisation.

It follows that, at least from a pathophysiological point of view, HBO should be initiated as soon as possible, even during rewarming, to limit the ischemia-reperfusion time. However, as impairment of microcirculation persists for many days after thawing [209],[210], and as it has been shown that the accompanying inflammatory cascade effects can be mitigated by HBO (as demonstrated in several models of ischemia-reperfusion injury [211]), the effects of delayed HBO can be considered "logical", even so that it is not possible to define a time period where HBO is to be considered "beyond utility" [212],[213].

A.9.4 Clinical Experience

Our own experience is relatively limited, as HBO is not generally recognised as a standard adjunctive treatment for frostbite. Over the past 15 years, only 8 cases were treated. All of them presented late, and had already advanced demarcation and sloughing of necrotic tissue. Cases referred to our hospital are primarily Belgian soldiers suffering injury during (sub) arctic training exercises, with a typical delay of 3 – 5 days, and civilian mountaineers who suffered injury either in the Himalayas or the Alps – with similar or longer delays to HBO. Our own therapeutic results are thus not any more significant than what has been reported before. However, we can confirm that HBO, when applied "lege artis", is a low-risk, well-tolerated treatment; a conservative treatment attitude (wait and see, amputate late) is still warranted. Early HBO clinically seems to provide a good and rapid separation of viable versus non-viable tissue. Magnetic resonance angiography one week after onset of injury seems promising in estimating the possibility of recovery of fingers or toes [109]. No randomised controlled human trials are available, and probably never will be.

A.10 SOFT TISSUE INFECTIONS – LIFE-THREATENING

A.10.1 Gas Gangrene

Gas gangrene is mostly caused by C. perfringens (80 – 90 %).

30% of all wounds are contaminated with C. perfringens, but only a few patients develop gas gangrene. Additionally, a decreased oxygen-reduction potential in the wound is required. This is mostly caused by circulatory failure. Most tissue destruction can be found in "high velocity"- wounds, e.g. bullet and blast wounds and vehicle accidents [144],[145],[146],[150]. Mechanisms responsible for the rapid tissue destruction in gas gangrene are not well understood. The most important factor for this is tissue hypoxia [137].

C. perfringens grows freely in oxygen tensions under 30mmHg. It produces 6 toxins. Alphatoxin is the most important one. It causes tissue necrosis. Thetatoxin leads to hemolysis, necrosis and cardiotoxicity [163],[164]. Clinical features are: pain, tachycardia, crepitus, hemolysis, low grade fever, bronzing of the skin, bullae formation, obtunded sensation [164].

A.10.1.1 Benefit of HBO

There are only a few studies as to the effects of HBO on gas gangrene. Animal models have not been established – except for one mouse model [158]. Studies on isolated bacteria have shown suppression of clostridial growth when oxygen pressure of 40 mmHg or more is applied. Oxygen pressure of 80 mmHg inhibits toxin synthesis. Spore formation is also suppressed [148],[151]. On the mouse model HBO did not improve the survival rate of patients with gas gangrene.

A.10.1.2 Clinical Scientific Evidence

Most data results from case reports, a lot from Eastern Europe and Russia. They are mostly on the scientific level of case reports or retrospective studies [131],[152]. When established within 24 hours after symptom onset HBO reduces the fatality of gas gangrene to about 5% [156]. Therapeutic regimen is the Boerema table: 20 m, 2 x 45 minutes [136]. HBO can be recommended on the basis of sound experimental evidence and favorable clinical experience [139],[147]. Additionally the therapy includes antibiotics, surgical debridements and intensive care therapy [155],[156].

A.10.2 Soft Tissue Infections and HBO

Soft tissue infections are an increasing medical problem. They occur after trauma, around foreign bodies and even spontaneously [162]. Clinical pictures vary widely (necrotizing fasciitis, Fournier gangrene, non-clostridial myonecrosis, etc.) and their etiology is multi-factorial. These infections are mostly caused by gram negative bacteria and anaerobic microorganisms. Streptococci play an important role [157].

Due to varying causes of infection the pathophysiology is not easy to describe. A common factor is tissue hypoxia that suppresses immunologic defence mechanisms [154]. Additionally there are host factors (reduced defence, vascular insufficiency, vein thrombosis). Bacteroidaceae have been shown to interfere with the host's interferon production and influence phagocytic activity.

A.10.2.1 Theoretical Benefit of HBO

In vitro HBO showed several effects on soft tissue infections:

- Bacteriostatic effects on anaerobic microorganisms (due to their inability to fight oxygen radicals), bactericidal effects (injury by free radicals) [151];
- Improvement of tissue oxygenation [154];
- Preventing extension of invading microorganisms [147];
- Improvement of phagocytic killing activity [154];
- Edema reduction [169];
- Increased function of capillaries [170]; and
- Increased efficacy of antibiotics (e.g. aminogylcosides, linezolid) [153].

In animal models (mouse, rat, rabbit) the mortality rates were significantly lower when treated with antibiotics and HBO. But (depending on the specific type of bacteria) there were also some harmful effects to be seen: streptococci infections worsen under high oxygen tensions [146].

A.10.2.2 Clinical Scientific Evidence

The level of evidence on soft tissue infections and HBO is low. There are only case reports and retrospective studies, no RCT. All most all study patients were compromised hosts [165],[166],[167],[168],[135].

HBO is one part of a multi-modal therapy and is only to be used for certain patients. The main therapeutic interventions for these patients are surgery, antimicrobial drugs and intensive care therapy. Data are contradictory. Risemann and lots of other authors found significantly reduced fatality and improved outcome, less number of debridements [138],[140],[161]. They recommend HBO should be used routinely in the treatment of necrotizing fasciitis. Some recent studies however showed no benefits for patients treated with HBO (no difference in survival, length of hospital stay or duration of antibiotic therapy) [142],[149]. This is supported by three studies from the early 1980's [171]. Further studies are required [141].

A.11 REFERENCES

[1] Baldwin TM. Tinnitus, a military epidemic: is hyperbaric oxygen therapy the answer? J. Spec. Oper. Med. 2009, 9: 33-43.

[2] http://www.hearinglossweb.com/Medical/Causes/nihl/mil/mil.htm. Hearing loss and military personnel. June 2006 – August 2011.

[3] Townsend M. Two-thirds of Afghan war veterans are suffering from hearing damage. The intense noise of the battlefield is afflicting British troops. The Observer 2009, 20 December. http://www.guardian.co.uk/uk/2009/dec/20/afghan-veterans-hearing-damage.

[4] Kemmer A, Stein T and Hierholzer C. Sudden Deafness. In: Handbook on Hyperbaric Medicine. Ed. D. Mathieu. Springer 2006: 451-468.

[5] Pilgramm M. Clinical and animal experiment studies to optimise the therapy for acute acoustic trauma. Scand. Audiol. Suppl. 1991, 34: 103-122.

[6] Lamm K and Arnold W. Successful treatment of noise-induced cochlear ischemia, hypoxia, and hearing loss. Ann. N.Y. Acad. Sci. 1991, 884: 233-248.

[7] D'Aldin C, Cherny L, Devriere F and Dancer A. Treatment of acoustic trauma. Ann. N.Y. Acad. Sci. 1999, 884: 328-344.

[8] Kuokkanen J, Aarnisalo AA and Ylikoski J. Efficiency of hyperbaric oxygen therapy in experimental acute acoustic trauma from firearms. Acta Otolaryngol. Suppl. 2000, 543: 132-134.

[9] Cakir BO, Ercan I, Civelek S, Korpinar S, Toklu AS, Gedik O, Isik G, Sayin I and Turgut S. Negative effect of immediate hyperbaric oxygen therapy in acute acoustic trauma. Otol. Neurotol. 2006, 27: 478-483.

[10] Narozny W. Influence of hyperbaric oxygen on the view of chicken's inner ear damage after exposure to wide-band noise. Otolaryngol. Pol. 2006, 60: 401-405.

[11] Colombari GC, Rossato M, Feres O and Hyppolito MA. Effects of hyperbaric oxygen treatment on auditory hair cells after acute noise damage. Eur. Arch. Otorhinolaryngol. 2011, 268: 49-56.

[12] Demaertelaere L and Van Opstal M. Treatment of acoustic trauma with hyperbaric oxygen. Acta Otorhinolaryngol. Belg. 1981, 35: 303-314.

[13] Pilgramm M and Schumann K. Hyperbaric oxygen therapy for acute acoustic trauma. Arch. Otorhinolaryngol. 1985, 241: 247-257.

[14] Lamm K, Lamm H and Arnold W. Effect of hyperbaric oxygen therapy in comparison to conventional or placebo therapy or no treatment in idiopathic sudden hearing loss, acoustic trauma, noise-induced hearing loss and tinnitus. A literature survey. Adv. Otorhinolaryngol. 1998, 54: 86-99.

[15] Winiarski M, Kantor I, Smereka J and Jurkiewicz D. Effectiveness of pharmacologic therapy combined with hyperbaric oxygen in sensorineural hearing loss following acute acoustic trauma. Preliminary report. Pol. Merkur Lekarski 2005, 19: 348-350.

[16] Lafere P, Vanhoutte D and Germonpre P. Hyperbaric oxygen therapy for acute noise-induced hearing loss: evaluation of different treatment regimens. Diving and Hyperbaric Medicine. 2010; 40: 63-7.

[17] Ylikoski J, Mrena R, Makitie A, Kuokkanen J, Pirvola U and Savolainen S. Hyperbaric oxygen therapy seems to enhance recovery from acute acoustic trauma. Acta Otolaryngol. 2008, 128: 1110-1115.

[18] http://www.oxynet.org/CostB14.htm. Information about the COST B14 Action "Hyperbaric Oxygen Therapy".

[19] http://www.echm.org/ECHM-Conferences.htm. European Committee for Hyperbaric Medicine. List of European Consensus Conferences.

[20] Benton PJ, Woodfine JD and Westwook PR. Arterial gas embolism following a 1-meter ascent during helicopter escape training. Aviat Space Environ Med 1996; 67: 63-64.

[21] Freund U, Kopolovic J and Durst AL. Compressed air emboli of the aorta and renal artery in blast injury. Injury 1980; 12: 37-38.

[22] Halpern P, Greenstein A, Melamed Y, Taitelman U, Sznajder I and Zveibil F. Arterial air embolism after penetrating lung injury. Crit Care Med 1983; 11: 392-393.

[23] Lee SY, Choi BI, Kim JS and Park KS. Paradoxical air embolism during hepatic resection. Br J Anaest. 2002; 88: 136-138.

[24] Frim DM, Wollman L, Evans AB and Ojemann RG. Acute pulmonary oedema after low-level air embolism during craniotomy. Case report. J Neurosurg 1996; 85: 937-940.

[25] Ries S, Knauth M, Kern R, Klingmann C, Daffertshofer M, Sartor K and Hennerici M. Arterial gas embolism after decompression: correlation with right-to-left shunting. Neurology 1999; 52: 401-404.

[26] Vesely TM. Air embolism during insertion of central venous catheters. J Vasc Intervent Radiology 2001; 12: 1291-1295.

[27] Butler BD and Hills BA. Transpulmonary passage of venous air emboli. J Appl Physiol 1990; 69: 237-244.

[28] Helps SC, Meyer-Witting M, Rilley PL and Gorman DF. The effect of gas emboli on rabbit cerebral blood flow. Stroke 1990; 21: 94-99.

[29] Pearson RR and Goad R.: Delayed cerebral oedema complicating cerebral arterial gas embolism. Case histories. Undersea Biomed Res 1982; 9: 283-296.

[30] Benson J, Adkinson C and Collier R. Hyperbaric oxygen therapy of iatrogenic cerebral arterial gas embolism. Undersea Hyperb Med 2003; 30: 117-126.

[31] Dexter F and Hindman BJ. Recommendations for hyperbaric oxygen therapy of cerebral air embolism based on a mathematical model of bubble absorption. Anesth Analg 1997; 84: 1203-7.

[32] Jain KK. Cerebral air embolism. In: Jain KK (Ed.). Textbook of Hyperbaric Medicine, 2nd ed. Kirkland WA: Hogrefe & Huber Publishers, 1996; 137-45.

[33] US Navy Diving Manual rev 6. Vol. 5. Diving Medicine and Recompression Chamber Operations. NAVSEA 0910-LP-106-0957. Washington, DC, USA: Naval Systems Command; 2008.

[34] Clarke D, Gerard W and Norris T. Pulmonary barotrauma-induced cerebral arterial gas embolism with spontaneous recovery: commentary on the rationale for therapeutic compression. Aviat Space Environm Med 2002; 73: 139-146.

[35] Ah-See AK. Review of arterial air embolism in submarine escape. In: Smith G, Editor. Proceedings of the 6th Int Congress on Hyperbaric Medicine. Aberdeen, Scotland: Aberdeen University Press; 1977; 349-351.

[36] Blanc P, Boussuges A, Henriette K, Sainty JM and Deleflie M. Iatrogenic cerebral air embolism: importance of an early hyperbaric oxygenation. Intensive Care Med 2002; 28: 559-563.

[37] Leitch DR and Green RD. Pulmonary barotrauma in divers and the treatment of cerebral arterial gas embolism. Aviat Space Environm Med 1986; 57: 931-938.

[38] Muth CM and Shank ES. Gas embolism. N Engl J Med. 2000; 342: 476-82.

[39] Layon AJ. Hyperbaric oxygen treatment for cerebral air embolism – Where are the data? (Editorial). Mayo Clin Proc 1991; 66: 641-6.

[40] Dutka AJ, Mink R, McDermott J, Clark JB and Hallenbeck JM. Effect of lidocaine on somatosensory evoked response and cerebral blood flow after canine cerebral air embolism. Stroke 1992; 23: 1515-21.

[41] Mitchell SJ, Benson M, Vadlamudi L and Miller P. Cerebral arterial gas embolism by helium: an unusual case successfully treated with hyperbaric oxygen and lidocaine. Ann Emerg Med. 2000 Mar; 35(3): 300-3.

[42] McDermott JJ, Dutka AJ, Koller WA and Flynn ET. Effects of an increased PO2 during recompression therapy for the treatment of experimental cerebral arterial gas embolism. Undersea Biomed Res 1992; 19: 403-13.

[43] Undersea and Hyperbaric Medical Society. UHMS Best Practice Guidelines: prevention and treatment of decompression sickness and arterial gas embolism. Durham, NC, USA, 2011.

[44] van Hulst RA, Drenthen J, Haitsma JJ, Lameris TW, Visser GH, Klein J and Lachmann B. Effects of hyperbaric treatment in cerebral air embolism on intracranial pressure, brain oxygenation, and brain glucose metabolism in the pig. Crit Care Med. 2005 April; 33(4): 841-6.

[45] Elliott DH and Moon RE. Manifestations of the decompression disorders. In: Bennett PB, Elloitt DH, Editors. The Physiology and Medicine of Diving. Philadelphia, PA, USA. WB Saunders, 1993; 481-505.

[46] McDermott JJ, Dutka AJ, Evans DE and Flynn ET. Treatment of experimental cerebral air embolism with lidocaine and hyperbaric oxygen. Undersea Biomed Res 1990; 17: 525-34.

[47] McDonald WS and Deitch EA. Hypertrophic skin grafts in burned patients: a prospective analysis of variables. J Trauma 27, 147-150 (1987).

[48] Monafo WW and Bessey PQ. Benefits and limitations of burn wound excision. World J Surg 16, 37-42 (1992).

[49] Staley M and Richard R. Management of the acute burn wound: an overview. Adv Wound Care 10, 39-44 (1997).

[50] Heimbach D, Engrav L, Grube B and Marvin J. Burn depth: a review. World J Surg 16, 10-15 (1992).

[51] Tredget EE and Yu YM. The metabolic effects of thermal injury. World J Surg 16, 68-79 (1992).

[52] Demling RH, Knox J, Youn YK and LaLonde C. Oxygen consumption early postburn becomes oxygen delivery dependent with the addition of smoke inhalation injury. J Trauma 32, 593-598; discussion 599 (1992).

[53] Jackson DM. Second thoughts on the burn wound. J Trauma 9, 839-862 (1969).

[54] Zawacki BE. The natural history of reversible burn injury. Surg Gynecol Obstet 139, 867-872 (1974).

[55] Zawacki BE. Reversal of capillary stasis and prevention of necrosis in burns. Ann Surg 180, 98-102 (1974).

[56] Arturson MG. The pathophysiology of severe thermal injury. J Burn Care Rehabil 6, 129-146 (1985).

[57] Arturson G and Jonsson CE. Transcapillary transport after thermal injury. Scand J Plast Reconstr Surg 13, 29-38 (1979).

[58] Lund T, Onarheim H and Reed RK. Pathogenesis of edema formation in burn injuries. World J Surg 16, 2-9 (1992).

[59] Lund T. The 1999 Everett Idris Evans memorial lecture. Edema generation following thermal injury: an update. J Burn Care Rehabil 20, 445-452 (1999).

[60] Ogle CK, Kong F and Guo X, et al. The effect of burn injury on suppressors of cytokine signalling. Shock 14, 392-398; discussion 398-399 (2000).

[61] Horton JW, Maass DL, White DJ, Sanders B and Murphy J. Effects of burn serum on myocardial inflammation and function. Shock 22, 438-445 (2004).

[62] D'Alesandro MM and Gruber DF. Quantitative and functional alterations of peripheral blood neutrophils after 10% and 30% thermal injury. J Burn Care Rehabil 11, 295-300 (1990).

[63] McCord JM. Oxygen-derived free radicals in postischemic tissue injury. N Engl J Med 312, 159-163 (1985).

[64] Oldham KT, Guice KS, Till GO and Ward PA. Activation of complement by hydroxyl radical in thermal injury. Surgery 104, 272-279 (1988).

[65] Friedl HP, Till GO, Trentz O and Ward PA. Role of oxygen radicals in tourniquet-related ischemia-reperfusion injury of human patients. Klin Wochenschr 69, 1109-1112 (1991).

[66] Schiller HJ, Andreoni KA and Bulkley GB. Free radical ablation for the prevention of post-ischemic renal failure following renal transplantation. Klin Wochenschr 69, 1083-1094 (1991).

[67] Noble R and Grossman R. Therapeutic HBO: help or hindrance in burn patients with CO poisoning? J Burn Care Rehabil 9, 581 (1988).

[68] Wells CH and Hilton JG. Effects of hyperbaric oxygen on post-burn plasma extravasation, in Hyperbaric Oxygen Therapy (Edited by J Davis and TK Hunt), pp. 259-265 (UHMS, Bethesda, MD, USA, 1977).

[69] Hart GB, O'Reilly RR and Broussard ND, et al. Treatment of burns with hyperbaric oxygen. Surg Gynecol Obstet 139, 693-696 (1974).

[70] Cianci P and Sato R. Adjunctive hyperbaric oxygen therapy in the treatment of thermal burns: A review. Burns 1994 Feb. 20(1):5-14.

[71] Kemmer A, Sauermuller G and Mentzel HE. Adjunctive hyperbaric oxygen in burns: preliminary experience in 12 patients. In XXVth Annual Meeting of EUBS (Eds A Shupak, R Lincoln and Y Grossman) 62-64 (Haifa, Israel, 1999).

[72] Korn HN, Wheeler ES and Miller TA. Effect of hyperbaric oxygen on second-degree burn wound healing. Arch Surg 112, 732-737 (1977).

[73] Germonpre P, Reper P and Vanderkelen A. Hyperbaric oxygen therapy and piracetam decrease the early extension of deep partial-thickness burns. Burns 22, 468-473 (1996).

[74] Bilic I, Petri NM and Bezic J, et al. Effects of hyperbaric oxygen therapy on experimental burn wound healing in rats: a randomized controlled study. Undersea Hyperb Med 32, 1-9 (2005).

[75] Shoshani O, Shupak A and Barak A, et al. Hyperbaric oxygen therapy for deep second degree burns: an experimental study in the guinea pig. Br J Plast Surg 51, 67-73 (1998).

[76] Ketchum SA, 3rd, Thomas AN and Hall AD. Effect of hyperbaric oxygen on small first, second, and third degree burns. Surg Forum 18, 65-67 (1967).

[77] Waisbren BA, Schutz D, Collentine G, Banaszak E and Stern M. Hyperbaric oxygen in severe burns. Burns Incl Therm Inj 8, 176-179 (1982).

[78] Brannen AL, Still J and Haynes M, et al. A randomized prospective trial of hyperbaric oxygen in a referral burn center population. Am Surg 63, 205-208 (1997).

[79] Ketchum SA, Thomas AN and Hall AD. Angiographic studies of the effect of hyperbaric oxygen on burn wound revascularisation. In IVth international congress of hyperbaric medicine (Eds J Wada and T Iwa) 388-394 (Bailliere, London, UK, 1970).

[80] Hammarlund C, Svedman C and Svedman P. Hyperbaric oxygen treatment of healthy volunteers with u.v.-irradiated blister wounds. Burns 17, 296-301 (1991).

[81] Niezgoda JA, Cianci P and Folden BW, et al. The effect of hyperbaric oxygen therapy on a burn wound model in human volunteers. Plast Reconstr Surg 99, 1620-1625 (1997).

[82] Stewart RJ, Yamaguchi KT and Cianci PA, et al. Effects of hyperbaric oxygen on adenosine triphosphate in thermally injured skin. Surg Forum 39, 87-90 (1988).

[83] Vaughan WG, Horton JW and White DJ. Burn induced cardiac dysfunction is reduced by pentoxifylline. Surg Gynecol Obstet 176, 459-468 (1993).

[84] Kawakami M, Endoh Y, Orringer EP and Meyer AA. Improvements in rheologic properties of blood by fluid resuscitation after burn injury in rats. J Burn Care Rehabil 13, 316-322 (1992).

[85] Niccole MW, Thornton JW, Danet RT, Bartlett RH and Tavis MJ. Hyperbaric oxygen in burn management: a controlled study. Surgery 82, 727-733 (1977).

[86] Hill GB and Osterhout S. Experimental effects of hyperbaric oxygen on selected clostridial species. I. In-vitro studies. J Infect Dis 125, 17-25 (1972).

[87] Knighton DR, Halliday B and Hunt TK. Oxygen as an antibiotic. The effect of inspired oxygen on infection. Arch Surg 119, 199-204 (1984).

[88] Allen DB, Maguire JJ and Mahdavian M, et al. Wound hypoxia and acidosis limit neutrophil bacterial killing mechanisms. Arch Surg 132, 991-996 (1997).

[89] Benhaim P and Hunt TK. Natural resistance to infection: leukocyte functions. J Burn Care Rehabil 13, 287-292 (1992).

[90] Heideman M and Bengtsson A. The immunologic response to thermal injury. World J Surg 16, 53-56 (1992).

[91] Bleser F and Benichoux R. Treatment of severe burns by hyperbaric oxygen. J Chir (Paris, France) 106, 281-290 (1973).

[92] Grossman AR. Hyperbaric oxygen in the treatment of burns. Ann Plast Surg 1, 163-171 (1978).

[93] Gorman D and Leitch I. The role of hyperbaric oxygen on thermal burn injuries: a brief review of the literature and the results of a pilot study. SPUMS J 18, 121-123 (1988).

[94] Niu AKC, Yang C and Lee HC. Burns treated with adjunctive hyperbaric oxygen therapy: a comparative study in humans. J Hyperb Med 2, 75-86 (1987).

[95] Cianci P, Williams C and Lueders H, et al. Adjunctive hyperbaric oxygen in the treatment of thermal burns. An economic analysis. J Burn Care Rehabil 11, 140-143 (1990).

[96] Germonpre P, Van Renterghem I, Vanderkelen A, Reper P and Duinslaeger L. Hyperbaric oxygen therapy in the treatment of burns: evaluation of systemic lipid peroxidation and activation of oxygen-radical dependent inflammatory reactions. In XXIInd Annual Meeting of EUBS (Eds A Marroni, G Oriani and F Wattel) 41-46 (Milan, Italy, 1996).

[97] Zamboni WA, Roth AC, Russell RC and Smoot EC. The effect of hyperbaric oxygen on reperfusion of ischemic axial skin flaps: a laser Doppler analysis. Ann Plast Surg 28, 339-341 (1992).

[98] Thom SR. Antagonism of carbon monoxide-mediated brain lipid peroxidation by hyperbaric oxygen. Toxicol Appl Pharmacol 105, 340-344 (1990).

[99] Kolski JM, Mazolewski PJ and Stephenson LL, et al. Effect of hyperbaric oxygen therapy on testicular ischemia-reperfusion injury. J Urol 160, 601-604 (1998).

[100] Xu N, Li Z and Luo X. Effects of hyperbaric oxygen therapy on the changes in serum sIL-2R and Fn in severe burn patients. Zhonghua Zheng Xing Shao Shang Wai Ke Za Zhi 15, 220-223 (1999).

[101] Grim PS, Nahum A and Gottlieb L, et al. Lack of measurable oxidative stress during HBO therapy in burn patients. Undersea Biomed Res 16 (Suppl.), 22 (1989).

[102] Tenenhaus M, Hansbrough JF, Zapata-Sirvent R and Neumann T. Treatment of burned mice with hyperbaric oxygen reduces mesenteric bacteria but not pulmonary neutrophil deposition. Arch Surg 129, 1338-1342 (1994).

[103] Akin ML, Gulluoglu BM and Erenoglu C, et al. Hyperbaric oxygen prevents bacterial translocation in thermally injured rats. J Invest Surg 15, 303-310 (2002).

[104] Stewart RJ, Mason SW and Taira MT, et al. Effect of radical scavengers and hyperbaric oxygen on smoke-induced pulmonary edema. Undersea Hyperb Med 21, 21-30 (1994).

[105] Hart GB, Strauss MB, Lennon PA and Whitcraft DD, 3rd. Treatment of smoke inhalation by hyperbaric oxygen. J Emerg Med 3, 211-215 (1985).

[106] Lind F. HBO in thermal burns. In 1st European Consensus Conference on Hyperbaric Medicine (Eds F Wattel and D Mathieu) 116-130 (Lille, France, 1994).

[107] Villanueva E, Bennett MH, Wasiak J and Lehm JP. Hyperbaric oxygen therapy for thermal burns. Cochrane Database Syst Rev. 3 (2004).

[108] Saunders PJ. Hyperbaric oxygen therapy in the management of carbon monoxide poisoning, osteoradionecrosis, burns, skin grafts, and crush injury. Int J Technol Assess Health Care 19, 521-525 (2003).

[109] Barker JR, Haws MJ, Brown RE, Kucan JO and Moore WD. Magnetic resonance imaging of severe frostbite injuries. Ann Plast Surg. 1997 March; 38(3): 275-9.

[110] Ray CS, Green B and Cianci P. Hyperbaric oxygen therapy in burn patients with adult respiratory distress syndrome. Undersea Biomed Res 1989; 16 (Suppl): 81.

[111] Cianci P, Slade JB Jr, Sato, RM and Faulkner J. Adjunctive hyperbaric oxygen therapy in the treatment of thermal burns. Undersea Hyperb Med 2013; 40: 98-108

[112] Uzun G, Sen H, Mutluoglu M, Kul M and Senol MG. Hyperbaric oxygen therapy for pediatric patients with carbon monoxide poisoning. The Turkish journal of pediatrics. 2009; 51(4): 403-4.

[113] Mutluoglu M, Uzun G, Eroglu M and Ay H. Domestic animals as a warning sign for carbon monoxide poisoning. Pediatric emergency care. 2012; 28(6): 596.

[114] Henry CR, Satran D, Lindgren B, Adkinson C, Nicholson CI and Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. JAMA: the journal of the American Medical Association. 2006; 295(4): 398-402.

[115] Satran D, Henry CR, Adkinson C, Nicholson CI, Bracha Y and Henry TD. Cardiovascular manifestations of moderate to severe carbon monoxide poisoning. Journal of the American College of Cardiology. 2005; 45(9): 1513-6.

[116] Choi IS. Delayed neurologic sequelae in carbon monoxide intoxication. Archives of neurology. 1983; 40(7): 433-5.

[117] Weaver LK, Hopkins RO, Chan KJ, Churchill S, Elliott CG and Clemmer TP, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. The New England journal of medicine. 2002; 347(14): 1057-67.

[118] Thom SR, Bhopale VM, Han ST, Clark JM and Hardy KR. Intravascular neutrophil activation due to carbon monoxide poisoning. American journal of respiratory and critical care medicine. 2006; 174(11): 1239-48.

[119] Brown AS, Moro MA, Masse JM, Cramer EM, Radomski M and Darley-Usmar V. Nitric oxide-dependent and independent effects on human platelets treated with peroxynitrite. Cardiovascular research. 1998; 40(2): 380-8.

[120] Thom SR. Leukocytes in carbon monoxide-mediated brain oxidative injury. Toxicology and applied pharmacology. 1993; 123(2): 234-47.

[121] Rothman SM, Thurston JH and Hauhart RE. Delayed neurotoxicity of excitatory amino acids in vitro. Neuroscience. 1987; 22(2): 471-80.

[122] Brown SD and Piantadosi CA. Recovery of energy metabolism in rat brain after carbon monoxide hypoxia. The Journal of clinical investigation. 1992; 89(2): 666-72.

[123] Domachevsky L, Adir Y, Grupper M, Keynan Y and Bentur Y. Hyperbaric oxygen in the treatment of carbon monoxide poisoning. Clinical toxicology. 2005; 43(3): 181-8.

[124] Thom SR. Carbon monoxide-mediated brain lipid peroxidation in the rat. Journal of applied physiology. 1990; 68(3): 997-1003.

[125] Thom SR. Functional inhibition of leukocyte B2 integrins by hyperbaric oxygen in carbon monoxide-mediated brain injury in rats. Toxicology and applied pharmacology. 1993; 123(2):248-56.

[126] Thom SR, Taber RL, Mendiguren, II, Clark JM, Hardy KR and Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. Annals of emergency medicine. 1995; 25(4): 474-80.

[127] Gorman DF, Clayton D, Gilligan JE and Webb RK. A longitudinal study of 100 consecutive admissions for carbon monoxide poisoning to the Royal Adelaide Hospital. Anaesthesia and intensive care. 1992; 20(3): 311-6.

[128] Raphael JC, Elkharrat D, Jars-Guincestre MC, Chastang C, Chasles V and Vercken JB, et al. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. Lancet. 1989; 2(8660): 414-9.

[129] Scheinkestel CD, Bailey M, Myles PS, Jones K, Cooper DJ and Millar IL, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. The Medical journal of Australia. 1999; 170(5): 203-10.

[130] Annane D, Chadda K, Gajdos P, Jars-Guincestre MC, Chevret S and Raphael JC. Hyperbaric oxygen therapy for acute domestic carbon monoxide poisoning: two randomized controlled trials. Intensive care medicine. 2011; 37(3): 486-92.

[131] Alvis HJ. Hyperbaric oxygen therapy of gas gangrene. JAMA 1971 (128). 445.

[132] Bartlett RL. Rabbit model of the use of fasciotomy and hyperbaric oxygenation in the treatment of compartment syndrome. UHM 1998 Suppl. 25.

[133] Boerema: life without blood. A study of the influence of high atmospheric pressure and hypothermia on diluation of the blood. J Cardiovasc Surg 1960 (1): 133-146.

[134] Bouachour G. Hyperbaric oxygen therapy in the management of crush injuries: a randomized double-blind placebo-controlled clinical trial. J Trauma 1996 (41): 333-339.

[135] Brown DR. A multicenter review of the treatment of major truncal necrotizing infections with and without hyperbaric oxygen therapy. Am J Surg 1994 (167): 485-489.

[136] Brummelkamp WK. Treatment of anaerobic infections (clostridial myonecrosis) by drenching the tissue with oxygen under high atmospheric pressure. Surgery 1961 (49): 299-302.

[137] Bryant AE. Clostridial gas gangrene, Cellular and molecular mechanisms of microvascular dysfunction induced by exotoxins of C. perfringens. J Infect Dis 2000 (182): 799-807.

[138] Clark LA. Hyperbaric oxygen in the treatment of life-threatening soft tissue infections. Resp. clin North America 1999 (5): 203-219.

[139] ECHM ETRS Ravenna 2006 Jury recommendations.

[140] Escobar SJ, Slade JB Jr, Hunt TK and Cianci P. Adjuvant hyperbaric oxygen therapy (HBO2) for treatment of necrotizing fasciitis reduces mortality and amputation rate. Undersea Hyperb Med. 2005 (32):437-443.

[141] Eskes A. Hyperbaric oxygen therapy for treating acute surgical and traumatic wounds. Cochrane review 2010.

[142] George ME. Hyperbaric oxygen does not improve outcome in patients with necrotizing soft tissue infections. Surg infections 2009 (10): 21-28.

[143] Gustilo RB. Problems in the management of type III open fractures, a new classification of type III open fractures. J Trauma 1984 (24): 742.

[144] Hart GB. Clostridial myonecrosis. The constant menace. Milit Med 1975 (140): 461-463.

[145] Hart GB. Gas gangrene. J Trauma 1983 (23): 991-1000.

[146] Herr M. Nekrotisierende Fasziitis. Update 2011. Unfallchirurg 2011 (114): 197-216.

[147] Hirn M. Hyperbaric oxygen in the treatment of gas gangrene and perineal necrotizing fasciitis. A clinical and experimental study. Eur J Surg 1993 (570): 1-36.

[148] Holland JA. Experimental and clinical experience with hyperbaric oxygen in the treatment of clostridial myonecrosis. Surgery 1975 (77): 75-85.

[149] Jallali N. Hyperbaric oxygen as adjuvant therapy in the management of necrotizing fasciitis. Am J Surg 2005 (198): 462-466.

[150] Johnson JT. Hyperbaric oxygen therapy for gas gangrene in war wounds. Am J Surg 1969 (118): 839-843.

[151] Kaye D. Effect of hyperbaric oxygen on clostridia in vitro and in vivo. Proc Soc Exp Biol med. 1967 (124): 360-366.

[152] Kindwall EP and Whelan HAT. Hyperbaric medicine practice 2004, Best Publishing Company, pp. 169-245; 549-574; 575-603; 753-779.

[153] Koomanachai P. Linezolid penetration into wound tissue of two diabetic patients before and after hyperbaric oxygen therapy. Unders Hyperb med 2011 (38): 11-16.

[154] Korhonen K. Hyperbaric oxygen therapy in acute necrotizing fasciitis with a special reference to tissue gas tensions. Ann chir et gyn 2000, Suppl. 214, 7-36.

[155] Korhonen K. Management of clostridial gas gangrene and the role of hyperbaric oxygen. Ann chir et gyn 1999 (88): 139-142.

[156] Lampl L. Hyperbare Oxygenation-Stellenwert in der Intensivtherapie. AINS 2009 (44): 652-658.

[157] Legbo JN. Necrotizing fasciitis: a comparative analysis of 56 cases. J Nat med Ass 2005 (97): 1692-1697.

[158] Muhvich KH. Evaluation of antimicrobials combined with hyperbaric oxygen in a mouse model of clostridial myonecrosis. J Trauma 1994 (36): 7-10.

[159] Murata I. Characteriziation of systemic and histologic injury after crush syndrome and intervals of reperfusion in a small animal model. J Trauma 2011 (70): 1453-1463.

[160] Myers RA. Hyperbaric oxygen therapy for trauma: crush injury, compartment syndrome and other traumatic peripheral ischemias. Intern Anaesth Clin 2000 (38): 139-151.

[161] Risemann JA. Hyperbaric oxygen therapy for necrotizing fasciitis and the need for debridements. Surgery 1990 (108): 847-850.

[162] Roje Z. Necrotizing fasciitis: literature review of contemporary strategies for diagnosing and management with three case reports. WJES 2011 (6): 46.

[163] Stevens DL. The role of clostridial toxins in the pathogenesis of gas gangrene. Clin Infect Dis 2002 (35, Suppl. 1): 93-100.

[164] Stevens DL. Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections. CID 2005: 41, 1373-1406.

[165] Sugihara A. The effect of hyperbaric oxygen therapy on the bout of treatment for soft tissue infections. J Infection 2004 (48): 330-333.

[166] Wagner S. Is intensive multimodality therapy the best treatment for Fournier gangrene? Evaluation of clinical outcome and survival rate of 41 patients. Surg Infect 2011 (12): 379-383.

[167] Weaver LK. Hyperbaric oxygen in the critically ill. Crit Care Med 2011 (39): 1784-1791.

[168] Wilkinson D. Hyperbaric oxygen treatment and survival from necrotizing soft tissue infection. Arch Surg 2004 (139): 1339-1345.

[169] Zamboni WA. Management of Fournier's gangrene and the role of hyperbaric oxygen. J Hyp med 1990 (5): 177-186.

[170] Zamboni WA, Roth AC, Russell RC, Graham B, Suchy H and Kucan JO. Morphologic analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. Plast Reconstr Surg. 1993 (91):1110-1123.

[171] Ziser A. Hyperbaric oxygen therapy for Fournier's gangrene. Crit Care Med 1985 (13): 773-774.

[172] Elliott DH and Kindwall EP. Decompression sickness. In: Kindwall EP, Whelan HT, Eds. Hyperbaric Medicine Practice. Flagstaff, AZ: Best Publishing Co., 1999, pp. 433-487.

[173] Boycott AE, Damant GC and Haldane JS. The prevention of compressed-air illness. J Hyg (Lond) 1908; 8: 342-43.

[174] DAN USA. Annual report on Decompression Illness, Diving Fatalities and Project Dive Exploration. Durham, NC, USA, Divers Alert Network, 2004.

[175] Francis TJR and Mitchell SJ. Manifestations of decompression disorders. In: Brubakk AO, Neuman TS, Eds. Bennett and Elliott's Physiology and Medicine of Diving. New York, Elsevier Science, 2003, pp. 578-599.

[176] Krause KM and Pilmanis AA. The effectiveness of ground level oxygen treatment for altitude decompression sickness in human subjects. Aviat Space Environm Med 2000; 71:115-118.

[177] Mitchell SJ, Doolette DJ, Wachholz CJ and Vann RD, Eds. Management of mild or marginal decompression sickness in remote locations. Durham, NC, USA, Divers Alert Network, 2005.

[178] Behnke AR and Shaw LA. The use of oxygen in the treatment of compressed air illness. US Navy Med Bull 1937; 35: 61-3.

[179] Goodman MW and Workman RD. Minimal recompression, oxygen-breathing approach to treatment of decompression sickness in divers and aviators. US Naval Experimental Diving Unit 1965; Report 5-65; 40 pp.

[180] UHMS Best Practice Guidelines, Prevention and Treatment of Decompression Sickness and Arterial Gas Embolism, 28 April 2011.

[181] Martin JD and Thom SR. Vascular leucocyte sequestration in decompression sickness and prophylactic hyperbaric oxygen therapy in rats. Aviat Space Environm Med 2002; 73: 565-569.

[182] Moon RE and Gorman DF. Treatment of the decompression disorders. In: Neuman TS, Brubakk AO, Editors. Bennett and Elliott's Physiology and Medicine of Diving. New York, NY, USA: Elsevier Science, 2003; pp. 600-650.

[183] Moon RE and Sheffield PJ. Guidelines for treatment of decompression illness. Aviat Space Environm Med 1997; 68: 234-243.

[184] Kizer KW. Delayed treatment of dysbarism: a retrospective review of 50 cases. JAMA 1982; 247: 2555-2558.

[185] Rudge FW and Shafer MR. The effect of delay on treatment outcome in altitude-induced decompression sickness. Aviat Space Environm Med 1991; 62: 687-690.

[186] Cianci P and Slade JB. Delayed treatment of decompression sickness with short, no-air break tables: review of 140 cases. Aviat Space Environ Med 2006; 77: 1003-8.

[187] Stipp W. Time to treatment for decompression illness. Research report RR 550, Norwich, UK, Health and Safety Executive Books, 2007, pp 1-29. Retrieved on December 2013 on http://www.hse.gov.uk/research/rrpdf/rr550.pdf.

[188] Blatteau JE, Gempp E, Simon O, Coulange M, Delafosse B, Souday V, Cochard G, Arvieux J, Henckes A, Lafere P, Germonpre P, Lapoussiere JM, Hugon M, Constantin P and Barthelemy A. Prognostic factors of spinal cord decompression sickness in recreational diving: retrospective and multicentric analysis of 279 cases. Neurocrit Care. 2011; 15: 120-127.

[189] Gempp E and Blatteau JE. Risk factors and treatment outcome in scuba divers with spinal cord decompression sickness. J Crit Care 2010; 25: 236-245.

[190] Divers Alert Network. The DAN annual review of recreational SCUBA diving injuries and fatalities based on 2003 data. Report on decompression illness, diving fatalities and project dive exploration. Durham, NC, USA, Divers Alert Network, 2005.

[191] Ball R. Effect of severity, time to recompression with oxygen, and retreatment on outcome of 49 cases of spinal cord decompression sickness. Undersea Hyperb Med 1993; 20: 133-145.

[192] Ross JAS. Clinical audit and outcome measures in the treatment of decompression illness in Scotland. A report to the National Health Service in Scotland Common Services Agency, National Services Division on the conduct and outcome of treatment for decompression illness in Scotland from 1991-1999. Aberdeen, UK: Department of Environmental and Occupational Medicine, University of Aberdeen Medical School, 2000.

[193] Hyldegaard, O, Kerem D and Melamed Y. Effect of combined recompression and air, oxygen, or heliox breathing on air bubbles in rat tissues. J Appl Physiol 2001; 90: 1639-1647.

[194] Drewry A and Gorman DF. A preliminary report on a prospective randomised double-blind controlled study of oxygen and oxygen-helium in the treatment of air diving decompression illness. Undersea Hyperbaric Med 1993; 20: 19-20.

[195] Moon RE. Hyperbaric oxygen treatment for decompression sickness. Undersea Hyperb Med 2014; 41: 151-154.

[196] Vann RD, Bute BP, Uggucioni DM and Smith LR. Prognostic factors in DCI in recreational divers. In: Moon RE; Sheffield PJ, Editors. Treatment of decompression illness. Kensington, MD. Undersea and Hyperbaric Medical Society, 1996; pp. 352-363.

[197] Bennett MH, Lehm JP, Mitchell SJ and Wasiak J. Recompression and adjunctive therapy for decompression illness. Cochrane Database Syst Rev. 2012; 5:CD005277.

[198] Mathieu D, Wattel F and Bakker D. Editors. Report of the 7th European Consensus Conference on Hyperbaric Medicine. Lille 2004; retrieved on December 10, 2013 at http://www.echm.org/documents/ECHM 7th Consensus Conference Lille 2004.pdf.

[199] Moon, RE. Editor. Adjunctive Therapy for Decompression Illness. Kensington, MD. Undersea and Hyperbaric Medical Society; 2003.

[200] Ledingham IM. Some clinical and experimental applications of high pressure oxygen. Proc R Soc Med. 1963; 56: 999-1002.

[201] Perrins ER and Bissonnette R. Frostbite, a new adjunct in treatment. JAMA. 1965; 194:211.

[202] Ward MP, Garnham JR, Simpson BR, Morley GH and Winter JS. Frostbite: general observations and report of cases treated by hyperbaric oxygen. Proc R Soc Med. 1968; 61(8): 787-789.

[203] Okuboye JA and Ferguson CC. The use of hyperbaric oxygen in the treatment of experimental frostbite. Can J Surg. 1968 January; 11(1): 78-84.

[204] Gage AA, Ishikawa H and Winter PM. Experimental frostbite and hyperbaric oxygenation. Surgery. 1969 December; 66(6): 1044-50.

[205] Hardenbergh E. Hyperbaric oxygen treatment of experimental frostbite in the mouse. J Surg Res. 1972 January; 12(1): 34-40.

[206] von Heimburg D, Noah EM, Sieckmann UP and Pallua N. Hyperbaric oxygen treatment in deep frostbite of both hands in a boy. Burns. 2001; 27(4): 404-408.

[207] Finderle Z and Cankar K. Delayed treatment of frostbite injury with hyperbaric oxygen therapy: a case report. Aviat Space Environ Med. 2002; 73(4): 392-394.

[208] McCrary B and Hursh TA. Hyperbaric Oxygen Therapy for a Delayed Frostbite Injury. Wounds. 2005; 17(12): 327-331.

[209] Bourne MH, Piepkorn MW, Clayton F and Leonard LG. Analysis of microvascular changes in frostbite injury. J Surg Res. 1986; 40(1): 26-35.

[210] Marzella L, Jesudass RR, Manson PN, Myers RA and Bulkley GB. Morphologic characterization of acute injury to vascular endothelium of skin after frostbite. Plast Reconstr Surg. 1989; 83(1): 67-75.

[211] Thom SR. Molecular mechanism for the antagonism of lipid peroxidation by hyperbaric oxygen. Undersea Biomed Res. 1990; 17(Suppl): 53-54.

[212] Zook N, Hussmann J and Brown R, et al. Microcirculatory studies of frostbite injury. Ann Plast Surg. 1998; 40(3): 246-255.

[213] Uygur F, Noyan N, Sever C and Gümüş T. The current analysis of the effect of hyperbaric oxygen therapy on the frostbitten tissue: Experimental study in rabbits. Central European Journal of Medicine. June 2009, Volume 4, Issue 2, pp. 198-202.

Annex B – HYPERBARIC CENTRES IDENTIFIED AS "SUITABLE" FOR TREATMENT OF MILITARY HBO INDICATIONS*

B.1 DEFINITIONS AND METHODS

The HBO centres and hospitals identified in the list below have been selected on the basis of personal knowledge of the local/regional situation, by the participants to the RTG-192 in the period between September and December 2012.

Wherever doubt existed as to the medical treatment capacities of the HBO centre (intensive HBO care, adjunctive care) or the adjoining/associated hospital, personal contact has been made in order to ascertain these facts. No formal agreements have been discussed at this stage as to the willingness of these HBO centres and/or hospitals to accept military patients and under which conditions of medical "control" and financial settlement, as these should be discussed on a case-by-case basis.

B.2 OTHER SOURCES

When identifying "new" HBO centres or updating information about centres already listed, the following resources may be useful.

B.2.1 Europe

- The OXYNET website, maintained by the European Committee for Hyperbaric Medicine (ECHM)
  http://www.oxynet.org
  http://www.echm.org
  Contact Email: office@echm.org
  Contact Telephone – Dr. J. KOT, Secretary General: +48 58 69 98 632
- Divers Alert Network Europe
  http://www.daneurope.org
  Contact Email: medical@daneurope.org
  Contact Telephone: +39 085 893 0333
- German Society for Diving and Hyperbaric Medicine (GTUeM)
  http://www.gtuem.org/33/Druckkammern.html
  Contact Email: gtuem@gtuem.org
  Contact Telephone: +49 8841 48 2167
- Advisory Committee for Hyperbaric Oxygen in Belgium (ACHOBEL)
  http://www.achobel.be/MemberList.htm
  Contact Email: mail@achobel.be
- Société de Médecine Hyperbare et Subaquatique (MedSubHyp)
  http://www.medsubhyp.com/site/caissons_militaires.htm

* List up-to-date as to December 2012.

- British Hyperbaric Association (BHA)
  http://www.hyperbaric.org.uk

B.2.2 United States

- Undersea and Hyperbaric Medical Society (UHMS)
  http://membership.uhms.org/?page=Accd_Facilities
  Contact Email: uhms@uhms.org
  Contact Telephone: +1 919 490 5140

B.3 HYPERBARIC FACILITIES

Table B-1: Hyperbaric Facilities and Hospitals.

HBO-Centre Name and Location (City)	Hosp. Based (Y / N)	Cooperating Hosp. Level	ICU	24/24	7/7	Special "Capabilities" of the Treating Hospital
Austria						
Graz University Hospital	Y	III	Y	Y	Y	University Hospital
Belgium (Source: www.achobel.be)						
Brussels, Military Hospital	Y	III	Y	Y	Y	Burn Centre
Charleroi, University Hospital	Y	II	Y	Y	Y	
Aalst, Onze-Lieve-Vrouw Ziekenhuis	Y	II	N	Y	Y	
Antwerpen, University Hospital UZA	Y	II	Y	Y	Y	
Brugge, AZ St.Jan Hospital	Y	II	N	Y	Y	
Genk, Z.O.L. Hospital	Y	II	N	Y	Y	
Liège, Citadelle Regional Hospital	Y	II	N	Y	Y	No emergency
Czech Republic						
Ostrava City Hospital	Y	II	Y	Y	Y	Septic surgery
Denmark						
Copenhagen	Y	III	Y	Y	Y	University Hospital
Aarhus	Y	III	?	Y	Y	Monoplace chamber ! University Hospital

HBO-Centre Name and Location (City)	Hosp. Based (Y / N)	Cooperating Hosp. Level	ICU	24/24	7/7	Special "Capabilities" of the Treating Hospital
Egypt						
Marsa Alam, Baromedical	N	I	N	Y	Y	Ambulatory-Diving Medicine
Safaga, General Hospital	Y	I (II)	N	Y	Y	Regional Hospital
Sharm-el Sheikh	Y	I (II)	N	Y	Y	El Nour Hospital
Sharm-el Sheikh	N	I	N	Y	Y	Private Chamber
France (Source: www.oxynet.org and http://www.medsubhyp.com)						
Lille, Centre Régional de Médecine Hyperbare – Hôpital Albert Calmette	Y	III	Y	Y	Y	Medical ICU
Marseille, CHU Sainte Marguerite	Y	II	Y	Y	Y	
Paris, Military Hospital Val de Grace	Y	II	Y	Y	Y	
Lyon, Hôpital Eduard Herriot	Y	III	Y	Y	Y	Neurosurgery
Toulon, HIA St Anne (Naval Hospital)	Y	II	Y	Y	Y	
Toulouse, CHU Purpan	Y	II	Y	Y	Y	University Hospital
Finland						
Turku University Hospital	Y	II	Y	Y	Y	
Helsinki, Medioxygen	N	II	N	Y	Y	
Germany (Source: www.gtuem.org and www.oxynet.org)						
Murnau Trauma Center	Y	III	Y	Y	Y	Trauma Center / Burn Center
Ulm Military Hospital	Y	III	Y	Y	Y	Trauma Center
Berlin Vivantes-Klinikum Friedrichshain	Y	III	Y	Y	Y	
Düsseldorf University Hospital	Y	III	Y	Y	Y	University Hospital
Traunstein Kreiskrankenhaus	Y	II	Y	Y	Y	

HBO-Centre Name and Location (City)	Hosp. Based (Y / N)	Cooperating Hosp. Level	ICU	24/24	7/7	Special "Capabilities" of the Treating Hospital
Germany (cont'd) (Source: www.gtuem.org and www.oxynet.org)						
Halle University Hospital	N (20 km)	III	Y	Y	Y	University Hospital
Kiel Naval Institute	N (5 km)	III	Y	Y	Y	University Hospital
Stuttgart DCS 1	N (5 km)	III	Y	Y	Y	Coop. with 2 Hospitals
München Druckkammer (Fire Brigade)	N	III	Y	Y	Y	Coop. with 3 large Hosp.
Minden Medicox	N	-	N	Y	Y	No Hospital coop.
Münster Amb. HBO	N	II	N	Y	Y	No emergency
Regensburg	N	III	N	Y	Y	No emergency
Greece (Source: www.oxynet.org)						
Thessaloniki, St. Paul's General Hospital	Y	II	Y	Y	Y	
Athens Naval Hospital	Y	II	Y	Y	Y	
Israel (Source: www.oxynet.org)						
Tel Aviv – Assaf Harofeh Medical Centre	Y	III	Y	Y	Y	
Haifa, Israel Naval Medical Institute	Y	III	Y	Y	Y	
Haifa, Elisha and Rambam Hospital's Hyperbaric and Diving Medical Centre	Y	II	N	Y	Y	
Eilat, Yoseftal Medical Center	N	II	N	Y	Y	
Italy						
Augusta (SR) Istituto Ortopedico "Villa Salus"	Y	II	Y	Y	Y	
Bari A.U.S.L. BA/4, O/C S. Paolo, Unit Operativa di Medicina Iperbarica	Y	II	Y	Y	Y	
Bolzano Iperbarico di Bolzano	N	II	N	Y	Y	

HBO-Centre Name and Location (City)	Hosp. Based (Y / N)	Cooperating Hosp. Level	ICU	24/24	7/7	Special "Capabilities" of the Treating Hospital
Italy (cont'd)						
Brescia (BS) Servizio OTI – Istituto Clinico Citt di Brescia	Y	II	Y	Y	Y	
Cagliari Centro di Medicina Iperbarica "G.Boero"	Y	II	Y	Y	Y	
Grosseto (GR) Servizio di Medicina Subacquea ed Iperbarica	N	II	N	Y	Y	
Pisa Azienda Ospedaliera Pisa	Y	II	Y	Y	Y	
Ravenna (RA) Centro Iperbarico srl	N	II	Y	Y	Y	
Roma (RM) Centro di Medicina Iperbarica	Y	III	Y	Y	Y	
Siracusa A.O. Umberto I UOC di Anestesia Rianimazione e Medicina Iperbarica	Y	II	Y	Y	Y	
Torino Servizio di Anestesia e Rianimazione	Y	II	Y	Y	Y	
Luxemburg						
Esch s/Alzette	Y	II	Y	Y	Y	
Maldives						
Bandos Medical Centre	N (boat)	II	N	Y	Y	Regional Hospital
Kuramathi	N (air)	II	N	Y	Y	Regional Hospital
Norway						
Bergen, Hyperbaric Medical Unit	Y	III	Y	Y	Y	Haukeland University Hospital
Oslo, Unit of Hyperbaric Medicine	Y	III	Y	Y	Y	Oslo University Hospital
Poland						
National Centre for Hyperbaric Medicine Gdynia	Y	III	Y	Y	Y	Septic surgery

HBO-Centre Name and Location (City)	Hosp. Based (Y / N)	Cooperating Hosp. Level	ICU	24/24	7/7	Special "Capabilities" of the Treating Hospital
Portugal (Source: www.oxynet.org)						
Lisbon, Naval Hospital	Y	II	Y	Y	Y	
Matosinhos, Hospital Pedro Hispano	Y	II	Y	Y	Y	
Funchal, Madeira	Y	II	Y	Y	Y	
Spain (Source: www.oxynet.org and http://www.cccmh.com/)						
CRIS-UTH Barcelona	Y	II	Y	Y	Y	Red Cross Hospital
Hospital General Castellon	Y	II	Y	Y	Y	
Medibarox Alicante	Y	II	Y	N	N	
Nuestra Senora Del Rosario Baleares	Y	II	Y	Y	Y	
Clinica El Angel – Malaga	Y	II	Y	Y	Y	
Medisub – Palma de Mallorca	Y	II	Y	Y	Y	
Valdecilla – Santander	Y	II	Y	Y	Y	
Sweden						
Stockholm, Karolinska Institutet	Y	III	Y	Y	Y	Burn Centre
Gothenburg, Sahlgrenska University Hospital	Y	II	Y	Y	Y	
Helsingborg, Hyperbaric Unit	Y	II	Y	Y	Y	
Switzerland						
Geneva University HBO Center	Y	III	Y	Y	Y	
Basel Hyperbaric Centre	N	–	N	N	N	No emergency
Netherlands						
Amsterdam, Academic Medical Centre	Y	III	Y	Y	Y	University Hospital
Den Helder, Navy hyperbaric centre	N	II	Y	Y	Y	

HBO-Centre Name and Location (City)	Hosp. Based (Y / N)	Cooperating Hosp. Level	ICU	24/24	7/7	Special "Capabilities" of the Treating Hospital
Netherlands (cont'd)						
Goes, Admiraal De Ruyter Hospital	Y	II	N	Y	Y	
Turkey						
İ.Ü. İstanbul Tıp Fakültesi, Sualtı Hekimliği ve Hiperbarik Tıp Anabilim Dalı Çapa, İstanbul	Y	II	Y	Y	Y	University Hospital
GATA Haydarpaşa Hastanesi, Sualtı Hekimliği ve Hiperbarik Tıp Servisi Selimiye, İstanbul	Y	II	Y	Y	Y	Teaching Hospital / Military
Sağlık Bakanlığı, Dr. Lütfi Kırdar Kartal Eğitim ve Araştırma Hastanesi Şemsi Denizer Cd. E5 Karayolu Cevizli Mevkii, 34890 Kartal / İstanbul	Y	III	Y	Y	Y	Teaching Hospital / Burn Center
GATA Sualtı Hekimliği ve Hiperbarik Tıp Anabilim Dalı Etlik / Ankara	Y	II	Y	Y	Y	Academy Hospital
United Kingdom (Source: http://www.hyperbaric.org.uk)						
Hull, North of England Medical Hyperbaric Unit	Y	II	Y	Y	Y	
London, Whipps Cross University Hospital	Y	II	Y	Y	Y	
Aberdeen Royal Infirmary	N	II	Y	Y	Y	
Chichester Hyperbaric Unit St Richard's Hospital	Y	II	Y	Y	Y	
Great Yarmouth East of England Hyperbaric Unit, James Paget Hospital	Y	II	Y	Y	Y	
Wirral, North West Emergency Recompression Unit, Murrayfield Hospital	Y	II	Y	Y	Y	

Annex C – HYPERBARIC REFERENCE PERSONS FOR MILITARY HBO*

AUSTRIA

Univ.-Prof.in Dr.in med.univ. Freyja-Maria Smolle-Juettner
University of Graz
Department of Surgery
Division of Thoracic and Hyperbaric Surgery
Auenbruggerplatz 29
8036 Graz
Tel: +43 385 13302
Email: freyja.smolle@)medunigraz.at

BELGIUM / LUXEMBURG

LtCol Peter Germonpré, MD
Medical Director
Centre for Hyperbaric Medicine
Military Hospital Brussels
Bruynstraat 1
B-1120 Brussels
Tel.: +32 2 264 4868
Email: peter.germonpre@mil.be

CZECH REPUBLIC

Michal Hajek, MD
Head of the Centre of Hyperbaric Medicine
City Hospital Ostrava
St. Nemocnicni 20
728 80 Ostrava
Tel.: +420 596 192 483, +420 596 192 484
Email: michal.hajek@mnof.cz
http://www.mnof.cz/centrum-hyperbaricke-mediciny--1061.html

Petr Dosel, MD
Deputy Director of the Institute of Aviation Medicine
Hyperbaric Facility located in Central Military Hospital
St. Gen. Piky 1
160 60 Prague 6
Tel.: +420 973 208 118 or +420 973 208 126
Email: petrdosel@atlas.cz
http://www.ulz.cz/en/hyperbaricka-oxygenoterapie/oddeleni/hyperbaricka-oxygenoterapie

* List up-to-date as to December 2012.

DENMARK

Erik Jansen, MD
University Hospital-Rigshospitalet
Department of Anaesthesiology
2100 Copenhagen
Tel.: +45 3545 3545
Email: erik.jansen@rh.regionh.dk

Mr. Peter Ric-Hansen
Naval and Diving Medical Section
Naval Station Copenhagen
Ved Sixtusbatteriet 2
1439 Copenhagen
Tel.: +45 32 66 45 01
Email: ric-hansen@dadlnet.dk

FINLAND

Mr. Tomi Wuorimaa
Diving Medical Centre
Centre of Military Medicine
P.O. Box 5
FI/02471 Upinniemi
Tel.: +358 299 580 370
Fax: +358 299 580 379
Email: tomi.wuorimaa@mil.fi

FRANCE

Pierre Louge, MD
Hôpital d'Instruction des Armées Sainte Anne
2 boulevard Sainte Anne
BCRM Toulon
BP 600
83800 Toulon Cedex 9
Tel.: +33 483 162342
Fax: +33 483 162705
Email: pierre.louge@orange.fr

Prof. Daniel Mathieu, MD, PhD
Urgence Respiratoire et Réanimation Médicale
Centre Hospitalier Régional Universitaire de Lille
2, avenue Oscar Lambret
59037 Lille Cedex
Tel.: +33 320 445550 or +33 320 445491
Fax: +33 320 444317
Email: dmathieu@chru-lille.fr

GERMANY

LtCol MC Dietmar M. Fischer, MD
Dept. of Anesthesiology and Intensive Care Medicine
Federal Armed Forces Hospital Ulm
Oberer Eselsberg 40
89081 Ulm
Tel.: +49 731 1710 2053 (ICU) or +49 731 1710 2001
Email: dietmarmanfredfischer@bundeswehr.org

ITALY

Gerardo Bosco
Universita degli Studie di Padova
Via Ugo Bassi
58/B, 35131 Padova
Tel.: +49 049 8275297
Email: gerardo.bosco@unipd.it

Dr. Med. Pasquale Longobardi
c/o Centro Iperbarico SRL
Via Augusto Torre 3
48126 Ravenna
Tel.: +39 0544 500152
Fax: +39 0544 500148
Mobile: +39 335 369120
Email: divedoc@libero.it

NETHERLANDS

Dr. P.J.A.M. van Ooij, MD, PhD
Department Diving and Submarine Medical Center
Royal Netherlands Navy
P.O. Box 10.000
1780 CA Den Helder
Tel.: +31 223 65 3076
Fax: +31 223 65 3148
Email: pjam.v.ooij.01@mindef.nl or duikerarts@home.nl

NORWAY

Professor Marit Grønning
National Centre for Diving Medicine
Dept. of Occupational Medicine
Haukeland University Hospital
5021 Bergen
Tel.: +47 55 97 3875
Mobile: +47 918 00 169
Email: marit.gronning@helse-bergen.no

POLAND

Dr. Med. Jacek Kot
National Centre for Hyperbaric Medicine
Institute of Maritime and Tropical Medicine
Medical University of Gdansk
Powstania Styczniowego 9B
81-519 Gdynia
Tel.: +48 586 998 632
Fax: +48 586 222 789
Email: jkot@gumed.edu.pl

PORTUGAL

CFR MN Franscisco Guerreiro, MD
Hospital da Marinha
Campo de Santa Clara
1149 Lisboa
Tel.: +351 21 884 0800
Email: quaresma.guerreiro@marinha.pt

SPAIN

Dr. Emilio Salas Pardo
Servicio de Medicine Subacuatica
C/Capitan Conforto S/N
Hospital Naval San Carlos
San Fernando, Cadiz E-11100
Tel: +34 9 56 59 81 00
Fax.: +34 9 56 59 81 25
Email: esalpar@oc.mde.es

SWEDEN

Surgeon Commander Carl Johanson
Swedish Armed Forces Medical Centre
P.O. Box 5155
Vastra Frolunda SE-426 0
Tel.: +46 31 69 26 62
Fax: +46 31 69 20 42
Email: carl.johanson@mil.se

TURKEY

LT(N) Gunalp Uzun, MD
Department of Underwater and Hyperbaric Medicine
Gulhane Military Medical Academy
Haydarpasa Teaching Hospital
34668 Uskudar, Istanbul
Tel.: +90 533 66 777 82
Email: gunalpuzun@gmail.com

Mesut Mutluoglu, MD
Department of Underwater and Hyperbaric Medicine
Gulhane Military Medical Academy
Haydarpasa Teaching Hospital
34668 Uskudar, Istanbul
Tel.: +90 533 66 777 82
Email: drmutluoglu@gmail.com

UNITED KINGDOM

Dr. Donald Thomas
Aberdeen Royal Infirmary
Foresterhill, Aberdeen AB25 2ZN
Tel.: +44 1224 553144
Email: donald.thomas@nhs.net

UNITED STATES

Capt Edward T. Waters, MC, USN
Director of Undersea Medicine and Radiation Health
Undersea Medicine Specialty Leader – Bureau of Medicine and Surgery
Undersea Medicine and Radiation Health (M3B3)
7700 Arlington Blvd.
Falls Church, VA 22042
Tel. (Office): +1 703-681-9275
Tel. (Cell): +1 202-445-0905
Fax: +1 703-681-5403
Email: edward.waters@med.navy.mil

REPORT DOCUMENTATION PAGE

1. Recipient's Reference	2. Originator's References	3. Further Reference	4. Security Classification of Document
	STO-TR-HFM-192 AC/323(HFM-192)TP/664	ISBN 978-92-837-2026-3	PUBLIC RELEASE

5. Originator

Science and Technology Organization
North Atlantic Treaty Organization
BP 25, F-92201 Neuilly-sur-Seine Cedex, France

6. Title

Optimal Use of Hyperbaric Oxygen Therapy in Military Medical Setting

7. Presented at/Sponsored by

The Task Group on Hyperbaric Oxygen Therapy in military medical setting explored the usefulness of hyperbaric oxygenation for medical conditions encountered in operational military settings; taking into account the technical specificities and constraints of hyperbaric oxygen therapy administration, recommendations are made as to the optimal implementation of this treatment.

8. Author(s)/Editor(s)	9. Date
Multiple	February 2016
10. Author's/Editor's Address	**11. Pages**
Multiple	84

12. Distribution Statement

There are no restrictions on the distribution of this document. Information about the availability of this and other STO unclassified publications is given on the back cover.

13. Keywords/Descriptors

Acoustic trauma
Anaerobic infections
Complex trauma
Diving accident treatment
Hyperbaric medicine
Hyperbaric Oxygen Therapy (HBO)
Medevac
Strategic evacuation planning
Submarine rescue planning
Treatment of battle wounds

14. Abstract

Hyperbaric Oxygen Therapy (HBO) is a treatment based on the respiration of high concentrations (up to 100%) of oxygen, while patients are exposed to high environmental pressures in a "hyperbaric chamber". This treatment has been shown to be beneficial in a number of conditions/injuries, some of which are pertinent to military-type injuries.

When administered timely and in a correct way, HBO improves the evolution and final outcome; however, because of the technical limitations of the treatment (necessity of a hyperbaric chamber, adequate oxygen and compressed air supplies, competent medical and paramedical personnel), HBO centers are not common, even in non-military setting.

The RTG-192 examined the possible military applications of HBO, and defined the conditions for its use. While not realistic to suggest the placement of HBO centers close to operations theatres, it may be possible to organize the medical evacuation routes in such a way that military patients can be treated in a (civilian or military) hyperbaric center "along the route", for a short period, before being further evacuated to their final destination.

Conditions and modalities for efficient use have been formulated, and recommendations have been made as to medical planning and education of military medical personnel.

NORTH ATLANTIC TREATY ORGANIZATION

SCIENCE AND TECHNOLOGY ORGANIZATION

BP 25
F-92201 NEUILLY-SUR-SEINE CEDEX • FRANCE
Télécopie 0(1)55.61.22.99 • E-mail mailbox@cso.nato.int

DIFFUSION DES PUBLICATIONS

STO NON CLASSIFIEES

Les publications de l'AGARD, de la RTO et de la STO peuvent parfois être obtenues auprès des centres nationaux de distribution indiqués ci-dessous. Si vous souhaitez recevoir toutes les publications de la STO, ou simplement celles qui concernent certains Panels, vous pouvez demander d'être inclus soit à titre personnel, soit au nom de votre organisation, sur la liste d'envoi.

Les publications de la STO, de la RTO et de l'AGARD sont également en vente auprès des agences de vente indiquées ci-dessous.

Les demandes de documents STO, RTO ou AGARD doivent comporter la dénomination « STO », « RTO » ou « AGARD » selon le cas, suivi du numéro de série. Des informations analogues, telles que le titre est la date de publication sont souhaitables.

Si vous souhaitez recevoir une notification électronique de la disponibilité des rapports de la STO au fur et à mesure de leur publication, vous pouvez consulter notre site Web (http://www.sto.nato.int/) et vous abonner à ce service.

CENTRES DE DIFFUSION NATIONAUX

ALLEMAGNE
Streitkräfteamt / Abteilung III
Fachinformationszentrum der Bundeswehr (FIZBw)
Gorch-Fock-Straße 7, D-53229 Bonn

BELGIQUE
Royal High Institute for Defence – KHID/IRSD/RHID
Management of Scientific & Technological Research
for Defence, National STO Coordinator
Royal Military Academy – Campus Renaissance
Renaissancelaan 30, 1000 Bruxelles

BULGARIE
Ministry of Defence
Defence Institute "Prof. Tsvetan Lazarov"
"Tsvetan Lazarov" bul no.2
1592 Sofia

CANADA
DGSIST
Recherche et développement pour la défense Canada
101 Colonel By Drive, 6 CBS
Ottawa, Ontario K1A 0K2

DANEMARK
Danish Acquisition and Logistics Organization
(DALO)
Lautrupbjerg 1-5
2750 Ballerup

ESPAGNE
SDGTECIN (DGAM)
C/ Arturo Soria 289
Madrid 28033

ESTONIE
Estonian National Defence College
Centre for Applied Research
Riia str 12
Tartu 51013

ETATS-UNIS
Defense Technical Information Center
8725 John J. Kingman Road
Fort Belvoir, VA 22060-6218

FRANCE
O.N.E.R.A. (ISP)
29, Avenue de la Division Leclerc
BP 72
92322 Châtillon Cedex

GRECE (Correspondant)
Defence Industry & Research General
Directorate, Research Directorate
Fakinos Base Camp, S.T.G. 1020
Holargos, Athens

HONGRIE
Hungarian Ministry of Defence
Development and Logistics Agency
P.O.B. 25
H-1885 Budapest

ITALIE
Centro Gestione Conoscenza
Secretariat General of Defence
National Armaments Directorate
Via XX Settembre 123/A
00187 Roma

LUXEMBOURG
Voir Belgique

NORVEGE
Norwegian Defence Research
Establishment
Attn: Biblioteket
P.O. Box 25
NO-2007 Kjeller

PAYS-BAS
Royal Netherlands Military
Academy Library
P.O. Box 90.002
4800 PA Breda

POLOGNE
Centralna Biblioteka Wojskowa
ul. Ostrobramska 109
04-041 Warszawa

PORTUGAL
Estado Maior da Força Aérea
SDFA – Centro de Documentação
Alfragide
P-2720 Amadora

REPUBLIQUE TCHEQUE
Vojenský technický ústav s.p.
CZ Distribution Information Centre
Mladoboleslavská 944
PO Box 18
197 06 Praha 9

ROUMANIE
Romanian National Distribution
Centre
Armaments Department
9-11, Drumul Taberei Street
Sector 6
061353 Bucharest

ROYAUME-UNI
Dstl Records Centre
Rm G02, ISAT F, Building 5
Dstl Porton Down
Salisbury SP4 0JQ

SLOVAQUIE
Akadémia ozbrojených síl gen.
M.R. Štefánika, Distribučné a
informačné stredisko STO
Demänová 393
031 06 Liptovský Mikuláš 6

SLOVENIE
Ministry of Defence
Central Registry for EU & NATO
Vojkova 55
1000 Ljubljana

TURQUIE
Milli Savunma Bakanlığı (MSB)
ARGE ve Teknoloji Dairesi
Başkanlığı
06650 Bakanliklar – Ankara

AGENCES DE VENTE

The British Library Document Supply Centre
Boston Spa, Wetherby
West Yorkshire LS23 7BQ
ROYAUME-UNI

Canada Institute for Scientific and Technical Information (CISTI)
National Research Council Acquisitions
Montreal Road, Building M-55
Ottawa, Ontario K1A 0S2
CANADA

Les demandes de documents STO, RTO ou AGARD doivent comporter la dénomination « STO », « RTO » ou « AGARD » selon le cas, suivie du numéro de série (par exemple AGARD-AG-315). Des informations analogues, telles que le titre et la date de publication sont souhaitables. Des références bibliographiques complètes ainsi que des résumés des publications STO, RTO et AGARD figurent dans le « NTIS Publications Database » (http://www.ntis.gov).

NORTH ATLANTIC TREATY ORGANIZATION

BP 25
F-92201 NEUILLY-SUR-SEINE CEDEX • FRANCE
Télécopie 0(1)55.61.22.99 • E-mail mailbox@cso.nato.int

SCIENCE AND TECHNOLOGY ORGANIZATION

DISTRIBUTION OF UNCLASSIFIED STO PUBLICATIONS

AGARD, RTO & STO publications are sometimes available from the National Distribution Centres listed below. If you wish to receive all STO reports, or just those relating to one or more specific STO Panels, they may be willing to include you (or your Organisation) in their distribution.

STO, RTO and AGARD reports may also be purchased from the Sales Agencies listed below.

Requests for STO, RTO or AGARD documents should include the word 'STO', 'RTO' or 'AGARD', as appropriate, followed by the serial number. Collateral information such as title and publication date is desirable.

If you wish to receive electronic notification of STO reports as they are published, please visit our website (http://www.sto.nato.int/) from where you can register for this service.

NATIONAL DISTRIBUTION CENTRES

BELGIUM
Royal High Institute for Defence – KHID/IRSD/RHID
Management of Scientific & Technological Research for Defence, National STO Coordinator
Royal Military Academy – Campus Renaissance
Renaissancelaan 30
1000 Brussels

BULGARIA
Ministry of Defence
Defence Institute "Prof. Tsvetan Lazarov"
"Tsvetan Lazarov" bul no.2
1592 Sofia

CANADA
DSTKIM
Defence Research and Development Canada
101 Colonel By Drive, 6 CBS
Ottawa, Ontario K1A 0K2

CZECH REPUBLIC
Vojenský technický ústav s.p.
CZ Distribution Information Centre
Mladoboleslavská 944
PO Box 18
197 06 Praha 9

DENMARK
Danish Acquisition and Logistics Organization (DALO)
Lautrupbjerg 1-5
2750 Ballerup

ESTONIA
Estonian National Defence College
Centre for Applied Research
Riia str 12
Tartu 51013

FRANCE
O.N.E.R.A. (ISP)
29, Avenue de la Division Leclerc – BP 72
92322 Châtillon Cedex

GERMANY
Streitkräfteamt / Abteilung III
Fachinformationszentrum der Bundeswehr (FIZBw)
Gorch-Fock-Straße 7
D-53229 Bonn

GREECE (Point of Contact)
Defence Industry & Research General Directorate, Research Directorate
Fakinos Base Camp, S.T.G. 1020
Holargos, Athens

HUNGARY
Hungarian Ministry of Defence
Development and Logistics Agency
P.O.B. 25
H-1885 Budapest

ITALY
Centro Gestione Conoscenza
Secretariat General of Defence
National Armaments Directorate
Via XX Settembre 123/A
00187 Roma

LUXEMBOURG
See Belgium

NETHERLANDS
Royal Netherlands Military Academy Library
P.O. Box 90.002
4800 PA Breda

NORWAY
Norwegian Defence Research Establishment, Attn: Biblioteket
P.O. Box 25
NO-2007 Kjeller

POLAND
Centralna Biblioteka Wojskowa
ul. Ostrobramska 109
04-041 Warszawa

PORTUGAL
Estado Maior da Força Aérea
SDFA – Centro de Documentação
Alfragide
P-2720 Amadora

ROMANIA
Romanian National Distribution Centre
Armaments Department
9-11, Drumul Taberei Street
Sector 6
061353 Bucharest

SLOVAKIA
Akadémia ozbrojených síl gen M.R. Štefánika, Distribučné a informačné stredisko STO
Demänová 393
031 06 Liptovský Mikuláš 6

SLOVENIA
Ministry of Defence
Central Registry for EU & NATO
Vojkova 55
1000 Ljubljana

SPAIN
SDGTECIN (DGAM)
C/ Arturo Soria 289
Madrid 28033

TURKEY
Milli Savunma Bakanlığı (MSB)
ARGE ve Teknoloji Dairesi Başkanlığı
06650 Bakanliklar – Ankara

UNITED KINGDOM
Dstl Records Centre
Rm G02, ISAT F, Building 5
Dstl Porton Down, Salisbury SP4 0JQ

UNITED STATES
Defense Technical Information Center
8725 John J. Kingman Road
Fort Belvoir, VA 22060-6218

SALES AGENCIES

The British Library Document Supply Centre
Boston Spa, Wetherby
West Yorkshire LS23 7BQ
UNITED KINGDOM

Canada Institute for Scientific and Technical Information (CISTI)
National Research Council Acquisitions
Montreal Road, Building M-55
Ottawa, Ontario K1A 0S2
CANADA

Requests for STO, RTO or AGARD documents should include the word 'STO', 'RTO' or 'AGARD', as appropriate, followed by the serial number (for example AGARD-AG-315). Collateral information such as title and publication date is desirable. Full bibliographical references and abstracts of STO, RTO and AGARD publications are given in "NTIS Publications Database" (http://www.ntis.gov).

ISBN 978-92-837-2026-3